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DATE: Thursday, October 18, 2007

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☐	L14	l7 and protein transduction domain	8
☐	L13	l8 and protein transduction domain	6
☐	L12	l8 near3 protein transduction domain	0
☐	L11	L10 not l9	4
☐	L10	L7 and HIV-TAT	10
☐	L9	L8 and HIV-TAT	6
☐	L8	LMP-1	382
☐	L7	LMP	2866
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☐	L5	6521750.pn.	1
☐	L4	7045614.pn.	1
☐	L3	6444803.pn.	1
☐	L2	6300127.pn.	1

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          patents
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          AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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=> s lnp
L1       470 LNP

=> s lmp
L2      4688 LMP

=> s l2 and HIV TAT
L3         6 L2 AND HIV TAT

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4         6 DUP REM L3 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L4  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2007 ACS on STN
AN  2007:563369  CAPLUS <<LOGINID::20071018>>
DN  147:1976
TI  Mechanisms of osteoinduction by ***LMP*** -1 (LIM mineralization
    protein-1), and a method of a co-therapeutic treatment of bone conditions
    by ***LMP*** and BMP agents
IN  Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA  Warsaw Orthopedic, Inc., USA; Emory University
SO  PCT Int. Appl., 126pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 4
    PATENT NO.         KIND  DATE        APPLICATION NO.      DATE
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PI  WO 2007058878      A2    20070524    WO 2006-US43610      20061109
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
           GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
           KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
           MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
           RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
           TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
           IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
           CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
           GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
           KG, KZ, MD, RU, TJ, TM
PRAI US 2005-736191P   P     20051110
AB  The present invention relates to the methods and compns. for the treatment
    of subjects having compromised bone conditions. Specifically, the
    invention relates to combinatorial therapeutic strategies including small
    mols. and peptidomimetics of LIM domain-contg. mineralization proteins
    (LMPs), particularly ***LMP*** -1 (LIM mineralization protein-1), to
    overcome the dose-related translational barriers for BMP-2 (bone
    morphogenetic protein 2) therapeutics. The inventors discovered that
    ***LMP*** -1 can increase cellular responsiveness of mesenchymal stem
    cells to BMP-2 and mechanistic elucidation of various aspects of the
    signaling pathway of ***LMP*** -1. It is further demonstrated that
    ***LMP*** -1 interacts in vitro an 85 kDa protein, identified as Smurf1,
    a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5.
    ***LMP*** -1 interaction occurs with the Smurf WW2 domain, and is
    dependent on a specific PY motif in ***LMP*** -1, and can be mimicked
    by a small peptide contg. only that motif. Further, ***LMP*** -1
    competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal
    degrdn. of Smads, contributing to an enhanced cellular responsiveness to
    BMP-2. Also ***LMP*** -1 is shown to interact with Jab1, an adaptor
    protein which regulates degrdn. of the Smad4 resulting in increased
    nuclear Smad4.

L4  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2007 ACS on STN
AN  2007:912734  CAPLUS <<LOGINID::20071018>>
DN  147:269173
TI  CAMK2 phosphorylation-related mechanism of osteoinduction by ***LMP***
    -3 (LIM domain-containing mineralization protein 3), and osteogenic
    compositions therefor
IN  Boden, Scott D.; Sangadala, Sreedhara
PA  USA
SO  U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 385,612.
    CODEN: USXXCO
DT  Patent
LA  English
FAN.CNT 4
    PATENT NO.         KIND  DATE        APPLICATION NO.      DATE
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PI  US 2007191591      A1    20070816    US 2006-633963       20061205
    US 2007027081      A1    20070201    US 2006-385612       20060321
PRAI US 2006-772322P   P     20060210
    US 2006-385612     A2    20060321
    US 2005-664073P    P     20050322
    US 2005-664074P    P     20050322
    US 2005-736191P    P     20051110
AB  The invention provides novel osteogenic compns. based on Smad ubiquitin
    regulatory factor-1 (Smurf1)-independent methods of osteoinduction using
    ***LMP*** -3 (LIM domain-contg. mineralization protein 3). The inventors
    discovered that a unique amino acid sequence (QNGCRPLTNSRSDRWSQMP)
in
    ***LMP*** -3 C-terminus contains a calmodulin kinase 2 (CAMK2)
    phosphorylation site (QNGCRPLTNSRSDRW). It was also discovered, that
    ***LMP*** -3 competes with Smad1 for phosphorylation by CAMK2. In a
```

broad aspect, the compn. comprises either a first amino acid sequence which is capable of being phosphorylated by CAMK2; or a nucleic acid sequence encoding the first amino acid sequence; or a combination thereof. Optionally, the first amino acid sequence may further comprise a second amino acid sequence which is capable of binding the Smurf1 protein. Further, the compn. may comprise a BMP (bone morphogenetic protein) and/or an agent capable of decreasing an amt. or an activity of CAMK2. The compns. of the instant invention may be incorporated into an implant or delivered via a catheter.

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:229584 CAPLUS <<LOGINID::20071018>>
DN 147:273365
TI A novel TAT fusion protein with osteoinductive activity
AU Zhang, Da-Wei; Li, Li-Wen; Hu, Yun-Yu
CS Institute of Orthopaedics, Xijing Hospital, The Fourth Military Medical University, Xian, 710032, Peop. Rep. China
SO Medical Hypotheses (2007), 68(5), 1009-1011
CODEN: MEHYDY; ISSN: 0306-9877
PB Elsevier Ltd.
DT Journal; General Review
LA English
AB A review. Summary: Osteoblasts are thought to be differentiated from pluripotent mesenchymal stem cells. Several intracellular and extracellular osteoinductive proteins are involved in this process. Such proteins include the bone morphogenetic proteins (BMPs) and the LIM mineralization proteins (LMPs) etc. ***LMP*** -1 is a novel LIM domain protein promoting the differentiation of osteoblasts during bone formation. It contains three LIM domains/motifs, one PDZ domain and a unique sequence. Through anal. of the amino acid sequence and the function of the LMPs, it has been found that the PDZ domain (1-93aa) and a unique region (94-133aa) appear to be crit. for bone formation. The TAT protein of human immunodeficiency virus can be fused with other macromols., peptides or proteins and transport them into cells successfully. Once being transduced into cells, the fusion protein can recover its biol. activity through being rapidly refolded. We supposed that TAT could be fused with ***LMP*** -1 (1-133aa) and ***LMP*** -1 (94-133aa) and the fusion proteins could be easily transduced through biol. membranes and generate biol. activity. The clin. application of BMPs has been limited for their relatively high cost and the unstable osteoinductivity. If the hypothesis proved to be practical, we would have a more effective new way to promote bone repair and regeneration.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of osteoinduction by ***LMP*** -1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by ***LMP*** and BMP agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-664073P	P	20050322		
US 2005-664074P	P	20050322		

AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly ***LMP*** -1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for BMP-2 (bone morphogenetic protein 2) therapeutics. ***LMP*** and BMP agents also include peptide or peptidomimetics-encoding oligonucleotides and ***LMP*** and BMP genes. The inventors discovered that ***LMP*** -1 can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to BMP-2 and mechanistic elucidation of various aspects of the signaling pathway of ***LMP*** -1. It is further demonstrated that ***LMP*** -1 interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5. ***LMP*** -1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in ***LMP*** -1, and can be mimicked by a small peptide contg. only that motif. Further, ***LMP*** -1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to BMP-2. Also ***LMP*** -1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1740600	A1	20070110	EP 2004-749433	20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007505621	T	20070315	JP 2006-526862	20040413
CN 1934123	A	20070321	CN 2004-80008027	20040413
IN 2005KN02097	A	20070810	IN 2005-KN2097	20051024
PRAI US 2003-456551P	P	20030324		
WO 2004-US9127	W	20040413		

AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , VP-22, a growth factor signal peptide sequence, Pep-1, etc.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:825023 CAPLUS <<LOGINID::20071018>>
DN 141:325787
TI Intracellular delivery expression construct encoding fusion protein of osteoinductive proteins and peptides and use to induce bone formation
IN Titus, Frances Louisa; Marx, Jeffrey C.; Boden, Scott D.; Yoon, Sangwook T.; Drapeau, Susan
PA USA
SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004197867	A1	20041007	US 2004-806915	20040323
CA 2517496	A1	20040924	CA 2004-2517496	20040324
AU 2004317501	A1	20051124	AU 2004-317501	20040324
PRAI US 2003-456551P	P	20030324		

AB The present invention provides a method of producing a cell-permeable osteoinductive polypeptide comprising introducing into a suitable host cell an expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide positioned so that the osteoinductive polypeptide is expressed as part of a fusion protein with the cell-permeable polypeptide. The invention also provides osteoinductive peptides which have demonstrated the ability to induce bone formation in vivo. The invention further relates to that the cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , VP-22, a growth factor signal peptide sequence, Pep-1, etc.

=> s lmp1
L5 2691 LMP1

=> s l5 or lmp 1
L6 4124 L5 OR LMP 1

=> s l6 and protein transduction domain

L7 6 L6 AND PROTEIN TRANSDUCTION DOMAIN

=> s bmp and protein transduction domain
L8 4 BMP AND PROTEIN TRANSDUCTION DOMAIN

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 4 DUP REM L8 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563369 CAPLUS <<LOGINID::20071018>>
DN 147:1976
TI Mechanisms of osteoinduction by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA Warsaw Orthopedic, Inc., USA; Emory University
SO PCT Int. Appl., 126pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058878	A2	20070524	WO 2006-US43610	20061109

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-736191P P 20051110
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptidomimetics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. The inventors discovered that LMP-1 can increase cellular responsiveness of mesenchymal stem cells to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912734 CAPLUS <<LOGINID::20071018>>
DN 147:269173
TI CAMK2 phosphorylation-related mechanism of osteoinduction by LMP-3 (LIM domain-containing mineralization protein 3), and osteogenic compositions therefor
IN Boden, Scott D.; Sangadala, Sreedhara
PA USA
SO U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 385,612.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007191591	A1	20070816	US 2006-633963	20061205
US 2007027081	A1	20070201	US 2006-385612	20060321

PRAI US 2006-772322P P 20060210
US 2006-385612 A2 20060321
US 2005-664073P P 20050322
US 2005-664074P P 20050322
US 2005-736191P P 20051110
AB The invention provides novel osteogenic compns. based on Smad ubiquitin regulatory factor-1 (Smurf1)-independent methods of osteoinduction using LMP-3 (LIM domain-contg. mineralization protein 3). The inventors discovered that a unique amino acid sequence (QNGCRPLTNSRSDRWSQMP) in LMP-3 C-terminus contains a calmodulin kinase 2 (CAMK2) phosphorylation site (QNGCRPLTNSRSDRW). It was also discovered, that LMP-3 competes with Smad1 for phosphorylation by CAMK2. In a broad aspect, the compn. comprises either a first amino acid sequence which is capable of being phosphorylated by CAMK2; or a nucleic acid sequence encoding the first amino acid sequence; or a combination thereof. Optionally, the first amino acid sequence may further comprise a second amino acid sequence which is capable of binding the Smurf1 protein. Further, the compn. may comprise a ***BMP*** (bone morphogenetic protein) and/or an agent capable of decreasing an amt. or an activity of CAMK2. The compns. of the instant invention may be incorporated into an implant or delivered via a catheter.

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of osteoinduction by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-664073P P 20050322
US 2005-664074P P 20050322
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. LMP and ***BMP*** agents also include peptide or peptidomimetics-encoding oligonucleotides and LMP and ***BMP*** genes. The inventors discovered that LMP-1 can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1740600	A1	20070110	EP 2004-749433	20040413

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

JP 2007505621 T 20070315 JP 2006-526862 20040413
CN 1934123 A 20070321 CN 2004-80008027 20040413
IN 2005KN02097 A 20070810 IN 2005-KN2097 20051024
PRAI US 2003-456551P P 20030324
WO 2004-US9127 W 20040413
AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, etc.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s BMP and HIV TAT
L10 6 BMP AND HIV TAT

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 6 DUP REM L10 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563369 CAPLUS <<LOGINID::20071018>>
DN 147:1976
TI Mechanisms of osteoinduction by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA Warsaw Orthopedic, Inc., USA; Emory University
SO PCT Int. Appl., 126pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058878	A2	20070524	WO 2006-US43610	20061109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2005-736191P P 20051110
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptidomimetics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. The inventors discovered that LMP-1 can increase cellular responsiveness of mesenchymal stem cells to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L11 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912734 CAPLUS <<LOGINID::20071018>>
DN 147:269173
TI CAMK2 phosphorylation-related mechanism of osteoinduction by LMP-3 (LIM domain-containing mineralization protein 3), and osteogenic compositions therefor
IN Boden, Scott D.; Sangadala, Sreedhara
PA USA
SO U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 385,612.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007191591	A1	20070816	US 2006-633963	20061205
US 2007027081	A1	20070201	US 2006-385612	20060321

PRAI US 2006-772322P P 20060210
US 2006-385612 A2 20060321
US 2005-664073P P 20050322
US 2005-664074P P 20050322
US 2005-736191P P 20051110
AB The invention provides novel osteogenic compns. based on Smad ubiquitin regulatory factor-1 (Smurf1)-independent methods of osteoinduction using LMP-3 (LIM domain-contg. mineralization protein 3). The inventors discovered that a unique amino acid sequence (QNGCRPLTNSRSDRWSQMP) in LMP-3 C-terminus contains a calmodulin kinase 2 (CAMK2) phosphorylation site (QNGCRPLTNSRSDRW). It was also discovered, that LMP-3 competes with Smad1 for phosphorylation by CAMK2. In a broad aspect, the compn. comprises either a first amino acid sequence which is capable of being phosphorylated by CAMK2; or a nucleic acid sequence encoding the first amino acid sequence; or a combination thereof. Optionally, the first amino acid sequence may further comprise a second amino acid sequence which is capable of binding the Smurf1 protein. Further, the compn. may comprise a ***BMP*** (bone morphogenetic protein) and/or an agent capable of decreasing an amt. or an activity of CAMK2. The compns. of the instant invention may be incorporated into an implant or delivered via a catheter.

L11 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of osteoinduction by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2005-664073P P 20050322
US 2005-664074P P 20050322
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. LMP and ***BMP*** agents also include peptide or peptidomimetics-encoding oligonucleotides and LMP and ***BMP*** genes. The inventors discovered that LMP-1 can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L11 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2005111058 A1 20051124 WO 2004-US9127 20040413
WO 2005111058 A9 20070118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1740600 A1 20070110 EP 2004-749433 20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
JP 2007505621 T 20070315 JP 2006-526862 20040413
CN 1934123 A 20070321 CN 2004-80008027 20040413
IN 2005KN02097 A 20070810 IN 2005-KN2097 20051024
PRAI US 2003-456551P P 20030324
WO 2004-US9127 W 20040413

AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , VP-22, a growth factor signal peptide sequence, Pep-1, etc.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:971289 CAPLUS <<LOGINID::20071018>>
DN 143:265304
TI Proliferative activity of extracellular HIV-1 Tat protein in human epithelial cells: Expression profile of pathogenetically relevant genes
AU Bettaccini, Alessia A.; Baj, Andreina; Accolla, Roberto S.; Basolo, Fulvio; Toniolo, Antonio Q.
CS Dipartimento di Scienze Cliniche e Biologiche, Universita dell' Insubria, Varese, Italy
SO BMC Microbiology (2005), 5, No pp. given
CODEN: BMMIBC; ISSN: 1471-2180
URL: http://www.biomedcentral.com/content/pdf/1471-2180-5-20.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English

AB Tat is being tested as a component of HIV vaccines. Tat activity has been mainly investigated on cells of lymphoid/hematopoietic lineages. HIV-1, however, is known to infect many different cells of both solid organs and mucosal surfaces. The activity of 2-exon (aa 1-101) and synthetic (aa 1-86) Tat was studied on mammary and amniotic epithelial cells cultured under low serum conditions. Small concns. of Tat (100 ng/mL) stimulated cell proliferation. Tat antibodies neutralized the mitogenic Tat activity. Changes of gene expression in Tat-treated cells were evaluated by RT-PCR and gene-array methods. Within 4 h of treatment, exposure to Tat is followed by up-regulation of some cell cycle-assocd. genes (transcription factors, cyclin/cdk complexes, genes of apoptotic pathways) and of genes relevant to HIV pathogenesis [chemokine receptors (CXCR4, CCR3), chemotactic cytokines (SDF-I, RANTES, SCYCI, SCYEI), IL6 family cytokines, inflammatory cytokines, factors of the TGF-.beta. family (TGFb, ***BMP*** -1, ***BMP*** -2)]. Upregulation of anti-inflammatory cytokines (IL-10, IL-19, IL-20), a hallmark of other persistent viral infections, was a remarkable feature of Tat-treated epithelial cell lines. Thus, extracellular Tat is mitogenic for mammary and amniotic epithelial cells and stimulates the expression of genes of pathogenic interest in HIV infection. These effects may favor virus replication and may facilitate the mother-to-child transmission of virus.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:825023 CAPLUS <<LOGINID::20071018>>
DN 141:325787
TI Intracellular delivery expression construct encoding fusion protein of osteoinductive proteins and peptides and use to induce bone formation
IN Titus, Frances Louisa; Marx, Jeffrey C.; Boden, Scott D.; Yoon, Sangwook T.; Drapeau, Susan
PA USA
SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004197867	A1	20041007	US 2004-806915	20040323
CA 2517496	A1	20040924	CA 2004-2517496	20040324
AU 2004317501	A1	20051124	AU 2004-317501	20040324
PRAI US 2003-456551P	P	20030324		

AB The present invention provides a method of producing a cell-permeable osteoinductive polypeptide comprising introducing into a suitable host cell an expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide positioned so that the osteoinductive polypeptide is expressed as part of a fusion protein with the cell-permeable polypeptide. The invention also provides osteoinductive peptides which have demonstrated the ability to induce bone formation in vivo. The invention further relates to that the cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , VP-22, a growth factor signal peptide sequence, Pep-1, etc.

=> d his

(FILE 'HOME' ENTERED AT 19:29:36 ON 18 OCT 2007)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 19:32:46 ON 18 OCT 2007
L1 470 S LNP
L2 4688 S LMP
L3 6 S L2 AND HIV TAT
L4 6 DUP REM L3 (0 DUPLICATES REMOVED)
L5 2691 S LMP1
L6 4124 S L5 OR LMP 1
L7 6 S L6 AND PROTEIN TRANSDUCTION DOMAIN
L8 4 S BMP AND PROTEIN TRANSDUCTION DOMAIN
L9 4 DUP REM L8 (0 DUPLICATES REMOVED)
L10 6 S BMP AND HIV TAT
L11 6 DUP REM L10 (0 DUPLICATES REMOVED)

=> s l2 or l6 or bmp
L12 25913 L2 OR L6 OR BMP

=> s l12 and (chimer? or fusion or hybrid or conjuga?)
L13 1365 L12 AND (CHIMER? OR FUSION OR HYBRID OR CONJUGA?)

=> s l13 and (bone form? or proteoglycan or different?)
L14 593 L13 AND (BONE FORM? OR PROTEOGLYCAN OR DIFFERENT?)

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15 354 DUP REM L14 (239 DUPLICATES REMOVED)

=> d bib abs

L15 ANSWER 1 OF 354 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1064219 CAPLUS <<LOGINID::20071018>>
TI Detection of gene expression by specific cell types in mixed samples or tissues such as mouse thymus cortex or medullary stromal cells using DGEM (***differential*** gene expression mapping)
IN Petrie, Howard T.
PA USA
SO PCT Int. Appl., 257pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007106507	A2	20070920	WO 2007-US6363	20070314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2006-782124P	P	20060314		

AB ***Differential*** gene expression mapping (DGEM) utilizes (1) laser capture microdissection or other methods of microdissection of the tissue regions of interest; (2) microarray screening of RNA isolated from the microdissected regions and anal. of purified individual cellular components from the tissue; (3) and computational profiling or subtraction to identify gene expression by specific cell types in situ. The method was applied to stromal cells from whole cortical and medullary regions of C57BL6 mouse thymus. As a result, DGEM, a reverse identification approach, solves previously insurmountable problems, as the lymphoid progenitors can be readily isolated, allowing fluctuations in receptor expression on lymphoid cells to be used to predict stratified stromal signals. An algorithmic approach can be used for calcg. the expression profile of a tissue/sample of interest that consists of at least two types of cells. Specifically, the approach electronically subtracts the expression profile of one component of a sample from the expression profile of the total sample, thus revealing the profiles of the other component. To confirm the robustness of the DGEM procedure, the gene expression profiles from each sample of whole medulla, whole cortex, cortical thymocytes and medullary thymocytes was sorted based only on the expression data.

=> s l15 and py<=2003
L16 167 L15 AND PY<=2003

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 167 ANSWERS - CONTINUE? Y/(N):n

=> d bib abs 1-10

L16 ANSWER 1 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2004:145930 BIOSIS <<LOGINID::20071018>>
DN PREV200400145749
TI Interactions between the ID and OLIG proteins mediate ***BMP*** effects on oligodendroglial ***differentiation*** .
AU Samanta, J. [Reprint Author]; Kessler, J. A. [Reprint Author]
CS Dept. Neurol, Northwestern Univ, Chicago, IL, USA
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (***2003***) Vol. 2003, pp. Abstract No. 781.2. http://sfn.scholarone.com. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003. Society of Neuroscience.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004
AB Bone Morphogenetic Proteins (BMPs) promote neuronal lineage commitment by cultured ventricular zone (VZ) progenitor cells but astrocytic commitment by subventricular zone (SVZ) progenitors. At all stages of development, the BMPs inhibit oligodendroglial (OL) lineage commitment both in vitro and in vivo. Treatment of cultured neural progenitor cells with BMP4 induces expression of all four members of the ID family of helix-loop-helix transcriptional inhibitors. Overexpression of ID4 and ID2 in SVZ progenitor cell inhibits OL lineage commitment. Conversely decreasing the levels of ID4 mRNA by RNA interference after BMP4 treatment significantly reduces the inhibitory effects of BMP4 on OL lineage commitment. Bacterial two- ***hybrid*** and coimmunoprecipitation studies demonstrate that ID4 and to a lesser extent ID2 complex with the OLIG proteins which are basic helix-loop-helix (bHLH) transcription factors expressed by OL progenitors. By contrast, ID1 and ID3 do not complex with the OLIG proteins. In addition, the OLIG and ID proteins both interact with E12 and E47. These observations suggest that the induction of ID4 and ID2 and their sequestration of both OLIG proteins and of E proteins such as E12 and E47 mediate the inhibitory effects of the BMPs on OL lineage commitment.

L16 ANSWER 2 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2004:78031 BIOSIS <<LOGINID::20071018>>
DN PREV200400079755
TI Identification and characterisation of two distinct Smad proteins from the fox-tapeworm Echinococcus multilocularis.
AU Zavala-Gongora, Ricardo; Kroner, Antje; Wittek, Britta; Knaus, Petra; Brehm, Klaus [Reprint Author]
CS Institute for Hygiene and Microbiology, University of Wuerzburg, Josef-Schneider-Strasse 2, D-97080, Wuerzburg, Germany kbrehm@hygiene.uni-wuerzburg.de
SO International Journal for Parasitology, (***December 2003***) Vol. 33, No. 14, pp. 1665-1677. print.
ISSN: 0020-7519 (ISSN print).
DT Article
LA English
ED Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB Members of the transforming growth factor-beta (TGF-beta) family of cytokines and their corresponding receptors regulate cellular key processes such as proliferation and ***differentiation*** , and could be involved in communication mechanisms between parasitic helminths and their hosts. A pivotal role in intracellular TGF-beta signalling is played by Smad factors which directly transmit incoming signals from the cell surface receptors to the nucleus. In this study, we have identified and characterised two novel members of the Smad family, EmSmadA and EmSmadB, which are expressed by the human parasite Echinococcus multilocularis. Based on amino acid sequence comparisons, both echinococcal Smad homologues could be classified as members of the R-Smad subfamily. EmSmadB showed a typical domain structure consisting of conserved MH1 and MH2 domains separated by a proline-rich linker region. EmSmadA, on the other hand, lacked an MH1 region and merely contained an MH2 domain, a feature which has so far not been described for R-Smads. Based on the structures of the corresponding chromosomal loci and on sequence features of the conserved L3 loop regions, EmSmadA and EmSmadB are most likely involved in the transmission of TGF-beta- and bone morphogenetic protein (***BMP***) signals, respectively. Yeast two- ***hybrid*** analyses revealed that both Echinococcus Smads are capable of homo- and heterodimer formations. However, while the formation of homodimers for EmSmadB required previous activation of the protein at the C-terminal SSVS motif, EmSmadA homodimers were already formed in the basal state of the factor. Upon expression of the Echinococcus Smads in human cells, EmSmadA, but not EmSmadB, was phosphorylated by the human TGF-beta type I receptor. Furthermore, both factors functionally interacted with human ***BMP*** receptors. By reverse transcriptase-PCR experiments, the encoding genes, emsmadA and emsmadB, were shown to be expressed in the larval stages metacestode and protoscolex during an infection of the intermediate host. Taken together, our data suggest an involvement of EmsmadA and EmsmadB in echinococcal developmental processes during natural infections and provide a solid basis for further investigations on TGF-beta signalling mechanisms in cestodes.

L16 ANSWER 3 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2004:71718 BIOSIS <<LOGINID::20071018>>
DN PREV200400073388
TI ***BMP*** induction of Id proteins suppresses ***differentiation*** and sustains embryonic stem cell self-renewal in collaboration with STAT3.
AU Ying, Qi-Long [Reprint Author]; Nichols, Jennifer; Chambers, Ian; Smith, Austin [Reprint Author]
CS Institute for Stem Cell Research, University of Edinburgh, West Mains Road, King's Buildings, Edinburgh, EH9 3JQ, UK qilong.ying@ed.ac.uk; austin.smith@ed.ac.uk
SO Cell, (***October 31 2003***) Vol. 115, No. 3, pp. 281-292. print.
CODEN: CELLB5. ISSN: 0092-8674.
DT Article
LA English
ED Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB The cytokine leukemia inhibitory factor (LIF) drives self-renewal of mouse embryonic stem (ES) cells by activating the transcription factor STAT3. In serum-free cultures, however, LIF is insufficient to block neural ***differentiation*** and maintain pluripotency. Here, we report that bone morphogenetic proteins (BMPs) act in combination with LIF to sustain self-renewal and preserve multilineage ***differentiation*** , ***chimera*** colonization, and germline transmission properties. ES cells can be propagated from single cells and derived de novo without serum or feeders using LIF plus ***BMP*** . The critical contribution of ***BMP*** is to induce expression of Id genes via the Smad pathway. Forced expression of Id liberates ES cells from ***BMP*** or serum dependence and allows self-renewal in LIF alone. Upon LIF withdrawal, Id-expressing ES cells ***differentiate*** but do not give rise to neural lineages. We conclude that blockade of lineage-specific transcription factors by Id proteins enables the self-renewal response to LIF/STAT3.

L16 ANSWER 4 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:577934 BIOSIS <<LOGINID::20071018>>
DN PREV200300583658
TI Sox6 regulation of cardiac myocyte development.
AU Cohen-Barak, Orit; Yi, Zanhua; Hagiwara, Nobuko; Monzen, Koshiro; Komuro, Issei; Brilliant, Murray H. [Reprint Author]
CS Department of Pediatrics, College of Medicine, Steele Memorial Children's Research Center, University of Arizona, 1501 N. Campbell Avenue, Tucson, AZ, 85724, USA mhb@peds.arizona.edu
SO Nucleic Acids Research, (***October 15 2003***) Vol. 31, No. 20, pp. 5941-5948. print.
ISSN: 0305-1048 (ISSN print).
DT Article
LA English
OS DDBJ-U32614; EMBL-U32614; GenBank-U32614
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB A mouse mutation (p100H/p100H) has been identified that is associated with cardioskeletal myopathy, heart block, delayed growth and early postnatal death. The gene that is disrupted in this mutation encodes the transcription factor Sox6. P19CL6 cells were used as an in vitro cardiomyocyte ***differentiation*** system and revealed that Sox6 is expressed exclusively when the cells are committed to ***differentiate*** to beating cardiac myocytes. We used the yeast two- ***hybrid*** system to identify the Prtb (Proline-rich transcript of the brain) protein as a Sox6 interactor, and subsequently confirmed the interaction by co-immunoprecipitation. Prtb expression in P19CL6 cells increased with ***differentiation*** to beating cardiomyocytes. Using the P19CL6 cells stably transfected with noggin, an antagonist of ***BMP*** (Bone Morphogenic Protein), we found that ***BMP*** expression is required for Sox6 expression in cardiomyocyte ***differentiation*** . Surprisingly, the expression of the alpha1c-subunit gene of the L-type Ca2+ channel decreased in P19CL6 cells as they ***differentiated*** to beating cardiac cells. Ectopic expression of Sox6 or Prtb alone in P19CL6 cells caused down-regulation of L-type Ca2+ alpha1c expression, but when Sox6 and Prtb were co-transfected to the cells, L-type Ca2+ alpha1c remained at basal levels. A similar relationship of Sox6 and L-type Ca2+ alpha1c expression was seen in vivo (comparing wild-type and p100H/p100H mutant mice). Thus, Sox6 is within the ***BMP*** pathway in cardiac ***differentiation*** , interacts with Prtb and may play a critical role in the regulation of a cardiac L-type Ca2+ channel.

L16 ANSWER 5 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:539678 BIOSIS <<LOGINID::20071018>>
DN PREV200300542028
TI Multiple functions of Noggin in cutaneous development: Leads and lessons from Noggin transgenic mice.
AU Sharov, A. [Reprint Author]; Weiner, L.; Sharova, T. [Reprint Author]; Siebenhaar, F. [Reprint Author]; Brissette, J.; Botchkarev, V. [Reprint Author]
CS Dermatology, Boston University School of Medicine, Boston, MA, USA
SO Journal of Investigative Dermatology, (***July 2003***) Vol. 121, No. 1, pp. 0828. print.
Meeting Info.: International Investigative Dermatology 2003 : Joint Meeting of the European Society for Dermatological Research, Japanese Society for Investigative Dermatology and Society for Investigative Dermatology. Miami Beach, Florida, USA. April 30-May 04, 2003. European Society for Dermatological Research.
ISSN: 0022-202X (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003

L16 ANSWER 6 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:485263 BIOSIS <<LOGINID::20071018>>
DN PREV200300485263
TI Enhancement of spine ***fusion*** using combined gene therapy and tissue engineering ***BMP*** -7-expressing bone marrow cells and allograft bone.
AU Hidaka, Chisa; Goshi, Kohei; Rawlins, Bernard; Boachie-Adjei, Obeneba; Crystal, Ronald G. [Reprint Author]
CS Department of Genetic Medicine, Weill Medical College of Cornell University, 520 East 70th Street, ST 505, New York, NY, 10021, USA geneticmedicine@med.cornell.edu
SO Spine, (***September 15 2003***) Vol. 28, No. 18, pp. 2049-2057. print.
ISSN: 0362-2436 (ISSN print).
DT Article
LA English
ED Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003
AB Study Design: Prospective study to assess the enhancement of spine ***fusion*** using a tissue engineering construct consisting of bone marrow cells genetically modified by adenovirus (Ad) vector-encoding bone morphogenetic protein-7 (***BMP*** -7) seeded onto an allograft scaffold in a rat model. Objectives: To evaluate Ad transgene expression at the ***fusion*** site and the effect of AdBMP-7-treatment on ***fusion*** rates, mechanical stability, microscopic anatomy, and ***bone*** ***formation*** rates. Summary of Background Data: Nonunion is a major complication of spine ***fusion*** . Gene transfer may be an effective method for locally overexpressing ***BMP*** -7, a gene important for ***bone*** ***formation*** and regeneration to enhance allograft spine ***fusion*** . Materials and Methods: Bone marrow cells were treated with AdBMP-7 or Adbetagal (encoding the marker gene beta-galactosidase), AdNull (with no gene), or no vector and implanted with allograft in a site of posterior spine ***fusion*** . Marker gene expression was assessed up to 14 days after administration. Fusions were evaluated at 8 weeks. Results: Ad gene expression was maximal on day 3, waning to background levels by 14 days. With AdBMP-7 treatment, radiographic ***fusion*** rate was 70% and mechanical ***fusion*** rate was 80% versus 0% by either parameter in control groups. Fused AdBMP-7-treated spines had a 2.5-fold to 3.0-fold lower range of motion and 1.7-fold to 1.9-fold lower hysteresis than controls. ***Fusion*** masses of AdBMP-7-treated spines had the microscopic appearance of normal trabecular bone and showed a 23-fold higher uptake of fluorochrome indicating increased ***bone*** ***formation*** . Conclusions: Addition of AdBMP-7-modified marrow cells can enhance allograft spine ***fusion*** .

L16 ANSWER 7 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:477719 BIOSIS <<LOGINID::20071018>>
DN PREV200300477719
TI Bone morphogenetic protein signalling in NGF-stimulated PC12 cells.
AU Althini, S.; Usoskin, D.; Kylberg, A.; ten Dijke, P.; Ebendal, T. [Reprint Author]
CS Department of Neuroscience, Unit for Developmental Neuroscience, Biomedical Centre, Uppsala University, SE-751 23, Box 587, Uppsala, Sweden Ted.Ebendal@neuro.uu.se
SO Biochemical and Biophysical Research Communications, (***August 1*** *** 2003***) Vol. 307, No. 3, pp. 632-639. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003
AB Bone morphogenetic proteins (BMPs) are shown to potentiate NGF-induced neuronal ***differentiation*** in PC12 phaeochromocytoma cells grown on collagen under low-serum conditions. Whereas, cell bodies remained rounded in control medium or with only BMPs present, addition of BMP4 or BMP6 robustly increased the neuritogenic effect of NGF within 2 days. NGF-increased phosphorylation of p44Erk1 and p42Erk2 between 2 and 24 h was unaffected by addition of BMP6. PC12 cells transfected with the SBE4x-luc reporter showed that BMP4 significantly increased receptor-activated Smad activity. Expression of constitutively active ***BMP*** receptor ALK2 activating Smad1 and Smad5 resulted in a strong increase in the SBE4x-luc reporter response. Adding the inhibitory Smad7 drastically reduced this signal. In contrast to wild-type (wt) Smad5, a Smad5 variant lacking five Erk phosphorylation sites in the linker region (designated Smad5/5SA) showed a strong background transcriptional activity. A ***fusion*** construct (Gal4-Smad5/5SA) was also highly transcriptionally active. Addition of the MEK inhibitor U0126 to PC12 cells expressing Gal4-Smad5/wt did not increase background transcriptional activity. However, upon activation by constitutively active ALK2 both Gal4-Smad5/wt and Gal4-Smad5/5SA strongly stimulated transcription. The data show that serine residues of the linker region of Smad5 reduce spontaneous transcriptional activity and that NGF-activated Erk does not antagonise ***BMP*** signalling at this site. Hence, NGF and ***BMP*** signals are likely to interact further downstream at the transcriptional level in neuronal ***differentiation*** of the PC12 cells.

L16 ANSWER 8 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:470611 BIOSIS <<LOGINID::20071018>>
DN PREV200300470611
TI Lumbar spinal ***fusion*** with a mineralized collagen matrix and rhBMP-2 in a rabbit model.
AU Liao, S. S.; Guan, K.; Cui, F. Z. [Reprint Author]; Shi, S. S.; Sun, T. S.
CS Biomaterials Laboratory, Department of Materials Science and Engineering, Tsinghua University, Beijing, 100084, China cuifz@mail.tsinghua.edu.cn
SO Spine, (***September 1 2003***) Vol. 28, No. 17, pp. 1954-1960. print.
ISSN: 0362-2436 (ISSN print).
DT Article
LA English
ED Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003
AB Study Design: A new mineralized collagen matrix combined with or without growth factor was used for the posterolateral spinal ***fusion*** in the rabbit lumbar spine. Objectives: The availability of a new osteoconductive matrix with or without recombinant osteoinductive growth factors offers a possible alternative to the use of autogenous bone for grafting indications. This study evaluated the ***bone*** - ***forming*** activity of the biomimetic matrix: nano-hydroxyapatite/collagen/polylactic acid (nHAC/PLA) combined without or with recombinant human bone morphogenetic protein-2 (rhBMP-2) in a rabbit posterolateral spinal ***fusion*** . Summary of Background Data: Many bone grafting materials such as titanium alloy, ceramics, and polymers were used to repair bony defects. However, each has specific disadvantaged. The permanent implantation still has possibility to be eroded in vivo, which is caused by late breakdown and abscess formation. The acidic outcome of polymer biodegradation was also negatively affected in the later-stage results of bone repair. It needed a promising material for an alternative to the use of autogenous bone for grafting indications. Materials and Methods: Sixty-four rabbits were randomly divided into four groups: autologous iliac crest bone group (ACB), nHAC/PLA composite group (nHAC/PLA), autologous iliac crest bone mixed with nHAC/PLA composite group (ACB+nHAC/PLA), nHAC/PLA composite with recombinant human ***BMP*** -2 group (nHAC/PLA+rhBMP-2). The lumbar intertransverse process fusions were assessed by manual palpation, radiographic, histologic, and mechanical strength, and scanning electronic microscopy (SEM) in a 10-week observation. Results: Optimal formulations of the ACB+nHAC/PLA and nHAC/PLA+rhBMP-2 groups were shown to perform similar to ACB in both the ***fusion*** ratio and mechanical strength in the 6 and 10 weeks after surgery. From the microstructure analysis of the samples, there was no negative effect when the compound implanted this composite with autogenous iliac crest, and there was also new bone-like tissue formation implanted this composite without combined rhBMP-2 early at the second week after surgery. Conclusions: This study shows the effective results of nHAC/PLA in rabbit posterolateral spinal ***fusion*** combined with rhBMP-2. It is an alternative method to autograft by compounding this osteoconductive matrix with growth factors.

L16 ANSWER 9 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:447576 BIOSIS <<LOGINID::20071018>>
DN PREV200300447576
TI ALK2 functions as a ***BMP*** type I receptor and induces Indian hedgehog in chondrocytes during skeletal development.
AU Zhang, Donghui; Schwarz, Edward M.; Rosier, Randy N.; Zuscik, Michael J.; Puzas, J. Edward; O'Keefe, Regis J. [Reprint Author]
CS Center for Musculoskeletal Research, Department of Orthopaedics, University of Rochester Medical Center, 601 Elmwood Avenue, Box 665, Rochester, NY, 14642, USA regis_okeefe@urmc.rochester.edu
SO Journal of Bone and Mineral Research, (***September 2003***) Vol. 18,

No. 9, pp. 1593-1604. print.
ISSN: 0884-0431 (ISSN print).
DT Article
LA English
ED Entered STN: 24 Sep 2003
Last Updated on STN: 24 Sep 2003
AB Growth plate chondrocytes integrate multiple signals during normal development. The type I ***BMP*** receptor ALK2 is expressed in cartilage and expression of constitutively active (CA) ALK2 and other activated type I ***BMP*** receptors results in maturation-independent expression of Ihh in chondrocytes in vitro and in vivo. The findings suggest that ***BMP*** signaling modulates the Ihh/PTHrP signaling pathway that regulates the rate of chondrocyte ***differentiation*** . Introduction: Bone morphogenetic proteins (BMPs) have an important role in vertebrate limb development. The expression of the ***BMP*** type I receptors BMPR-IA (ALK3) and BMPR-IB (ALK6) have been more completely characterized in skeletal development than ALK2. Methods: ALK2 expression was examined in vitro in isolated chick chondrocytes and osteoblasts and in vivo in the developing chick limb bud. The effect of overexpression of CA ALK2 and the other type I ***BMP*** receptors on the expression of genes involved in chondrocyte maturation was determined. Results: ALK2 was expressed in isolated chick osteoblasts and chondrocytes and specifically mediated ***BMP*** signaling. In the developing chick limb bud, ALK2 was highly expressed in mesenchymal soft tissues. In skeletal elements, expression was higher in less mature chondrocytes than in chondrocytes undergoing terminal ***differentiation*** . CA ALK2 misexpression in vitro enhanced chondrocyte maturation and induced Ihh. Surprisingly, although parathyroid hormone-related peptide (PTHrP) strongly inhibited CA ALK2 mediated chondrocyte ***differentiation*** , Ihh expression was minimally decreased. CA ALK2 viral infection in stage 19-23 limbs resulted in cartilage expansion with joint ***fusion*** . Enhanced periarticular expression of PTHrP and delayed maturation of the cartilage elements were observed. In the cartilage element, CA ALK2 misexpression precisely colocalized with the expression with Ihh. These findings were most evident in partially infected limbs where normal morphology was maintained. In contrast, ***BMP*** -6 had a normal pattern of ***differentiation*** -related expression. CA BMPR-IA and CA BMPR-IB overexpression similarly induced Ihh and PTHrP. Conclusions: The findings show that ***BMP*** signaling induces Ihh. Although the colocalization of the activated type I receptors and Ihh suggests a direct ***BMP*** -mediated signaling event, other indirect mechanisms may also be involved. Thus, while BMPs act directly on chondrocytes to induce maturation, this effect is counterbalanced in vivo by induction of the Ihh/PTHrP signaling loop. The findings suggest that BMPs are integrated into the Ihh/PTHrP signaling loop and that a fine balance of ***BMP*** signaling is essential for normal chondrocyte maturation and skeletal development.

L16 ANSWER 10 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:431343 BIOSIS <<LOGINID::20071018>>
DN PREV200300431343
TI Smad1C, a Hoxc-8 interacting domain of Smad1, augments bone mineral density in transgenic mice.
AU Liu, Z. [Reprint Author]; Shi, W. [Reprint Author]; Sun, C. [Reprint Author]; Nagy, T. [Reprint Author]; Lu, C. [Reprint Author]; Jee, W. S. S.; Ji, X.; Wu, Y. [Reprint Author]; Shi, X. [Reprint Author]; Li, O. [Reprint Author]; Cao, X. [Reprint Author]
CS Pathology, University of Alabama at Birmingham, Birmingham, AL, USA
SO Journal of Bone and Mineral Research, (***September 2002***) Vol. 17, No. Suppl 1, pp. S195. print.
Meeting Info.: Twenty-Fourth Annual Meeting of the American Society for Bone and Mineral Research. San Antonio, Texas, USA. September 20-24, 2002.
American Society for Bone and Mineral Research.
ISSN: 0884-0431 (ISSN print).
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003

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L16 ANSWER 11 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:425169 BIOSIS <<LOGINID::20071018>>
DN PREV200300425169
TI ***LMP1*** , a viral relative of the TNF receptor family, signals principally from intracellular compartments.
AU Lam, Ngan; Sugden, Bill [Reprint Author]
CS McArdle Laboratory for Cancer Research, University of Wisconsin-Madison, 1400 University Avenue, Madison, WI, 53706, USA
sugden@oncology.wisc.edu
SO EMBO (European Molecular Biology Organization) Journal, (***June 16*** *** 2003***) Vol. 22, No. 12, pp. 3027-3038. print.
ISSN: 0261-4189 (ISSN print).
DT Article
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003
AB Latent membrane protein 1 (***LMP1***) is an Epstein-Barr virus (EBV)-encoded, ligand-independent receptor that mimics CD40. We report here that ***LMP1*** signals principally from intracellular compartments. ***LMP1*** associates simultaneously with lipid rafts and with its signaling molecules, tumor necrosis factor-receptor (TNF-R)-associated factors (TRAFs) and TNF-R1-associated death domain protein (TRADD) intracellularly, although it can be detected at low levels at the plasma membrane, indicating that most of ***LMP1*** 's signaling complex resides in intracellular compartments. ***LMP1*** 's signaling is independent of its accumulation at the plasma membrane in ***different*** cells, and as demonstrated by a mutant of ***LMP1*** which has significantly reduced localization at the plasma membrane yet signals as efficiently as does wild-type ***LMP1*** . The ***fusion*** of the transmembrane domain of ***LMP1*** to signaling domains of CD40, TNF-R1 and Fas activates their signaling; we demonstrate that a ***fusion*** of ***LMP1*** with CD40 recruits TRAF2 intracellularly. Our results imply that members of the TNF-R family can signal from intracellular compartments containing lipid rafts and may do so when they act in autocrine loops.

L16 ANSWER 12 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:352897 BIOSIS <<LOGINID::20071018>>
DN PREV200300352897
TI In vivo ***bone*** ***formation*** in fracture repair induced by direct retroviral-based gene therapy with bone morphogenetic protein-4.
AU Rundle, Charles H.; Miyakoshi, Naohisa; Kasukawa, Yuji; Chen, Shin-Tai; Sheng, Matilda H.-C.; Wergedal, Jon E.; Lau, K.-H. William; Baylink, David J. [Reprint Author]
CS Departments of Medicine and Biochemistry, Musculoskeletal Disease Center, Loma Linda University, Jerry L. Pettis Memorial Veterans Administration Medical Center, 11201 Benton Street, 151, Loma Linda, CA, 92357, USA
David.Baylink@med.va.gov
SO Bone (New York), (***June 2003***) Vol. 32, No. 6, pp. 591-601. print.
CODEN: BONEDL. ISSN: 8756-3282.
DT Article
LA English
ED Entered STN: 30 Jul 2003
Last Updated on STN: 30 Jul 2003
AB This study sought to develop an in vivo gene therapy to accelerate the repair of bone fractures. In vivo administration of an engineered viral vector to promote fracture healing represents a potential high-efficacy, low-risk procedure. We selected a murine leukemia virus (MLV)-based retroviral vector, because this vector would be expected to target transgene expression to the proliferating periosteal cells arising shortly after bone fracture. This vector transduced a ***hybrid*** gene that consisted of a bone morphogenetic protein (***BMP***)-4 transgene with the ***BMP*** -2 secretory signal to enhance the secretion of mature ***BMP*** -4. The MLV vector expressing this ***BMP*** -2/4 ***hybrid*** gene or beta-galactosidase control gene was administered at the lateral side of the fracture periosteum at 1 day after fracture in the rat femoral fracture model. X-ray examination by radiograph and peripheral quantitative computed tomography at 7, 14, and 28 days, after fracture revealed a highly significant enhancement of fracture tissue size in the MLV- ***BMP*** -2/4-treated fractures compared to the control fractures. The tissue was extensively ossified at 14 and 28 days, and the newly formed bone exhibited normal bone histology. This tissue also exhibited strong immunohistochemical staining of ***BMP*** -4. Additional control and MLV- ***BMP*** -2/4-treated animals each were monitored for 70 days to determine the fate of the markedly enhanced fracture callus. Radiographs showed that the hard callus had been remodeled and substantial healing at the fracture site had occurred, suggesting that the union of the bone at the fracture site was at least as high in the ***BMP*** -4-treated bone as in the control bone. There was no evidence of viral vector infection of extraskeletal tissues, suggesting that this in vivo gene therapy for fracture repair is safe. In summary, we have demonstrated for the first time that a MLV-based retroviral vector is a safe and effective means of introducing a transgene to a fracture site and that this procedure caused an enormous augmentation of fracture ***bone*** ***formation*** .

L16 ANSWER 13 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:336815 BIOSIS <<LOGINID::20071018>>
DN PREV200300336815
TI Identification of IGF2 as a Potential Target Gene of the Pbx1-Homeobox Protein by In-Vitro ***Differentiation*** of Homozygous Pbx1 Knock-Out ES Cells.
AU Scheele, Jurgen S. [Reprint Author]; Jurgens, Anne S. [Reprint Author]; Zemojtel, Tomasz C. [Reprint Author]; Sykes, David B. [Reprint Author]; Kamps, Mark P. [Reprint Author]; Kolanczyk, Mateusz K. [Reprint Author]
CS Div. of Hematology/Oncology, University Freiburg, Medical Center, Freiburg, Germany
SO Blood, (***November 16 2002***) Vol. 100, No. 11, pp. Abstract No. 2118. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB In 25% of pediatric pre-B ALL the t(1,19) chromosome translocation leads to a ***fusion*** gene consisting of the transcriptional activator E2A and the homeobox gene pbx1. Pbx1 knock-out mice were recently reported to die on gestation day 15 from severe hypoplasia or aplasia of multiple organs. Pbx1 nullizygous embryos exhibited diffuse patterning defects, but only in domains specified by Hox paralogs that bear the Pbx dimerization motif. In the rat brain pbx1 expression is detected as early as day 14 p.c., increases until day 17 and is most abundant during the first postnatal week. Interestingly Pbx1 is expressed in regions of active neurogenesis. First in the neocortex and midbrain, later in subventricular zone and olfactory bulbs, where pbx1 brain expression persists until adulthood. Since pbx1 nulizygous mice die on day 15 the questions about Pbx1 function in the postnatal brain can be only addressed with the help of conditional knock-out technology and through in vitro studies. Utilizing the Cre-lox system we obtained both single and double allele knock-outs of the pbx1 gene in murine Embryonic Stem (ES) cells. We induced neuronal ***differentiation*** of wt and pbx1 knockout ES cells by the aggregation method and 9-cis 13-cis all trans retinoic acid (RA) treatment. To study ***differential*** gene expression changes during ***differentiation*** we collected RNA material from cultured cells up to the 9th day after reattachment of the embryoid bodies (EB) onto the gelatinized cell culture dishes. Previously identified target genes of the Pbx1-homologue Extradenticle (Exd) include members of the Wnt and TGF-b/ ***BMP*** families. Studies of E2a-Pbx1 oncogene transactivation properties in ***different*** cellular backgrounds reveal WNT and FGF family members as potential targets. Therefore transcripts we compared by RT-PCR did not only include previously described neural and mesodermal lineage marker genes but also WNT and FGF gene families members. Expression of neuronal and repression of mesodermal genes coincided with increased neuronal and glial cell yields observed by immunohistochemistry in pbx1 knock-out cells in comparison to wildtype cells. Microarray experiments with the affymetrix system did not only confirm the results from RT-PCR and immunhistochemistry but revealed at least 10 ***differentially*** expressed genes with potential functions in regulation of growth and ***differentiation*** . Among the ***differentially*** expressed genes with a potential growth regulatory function we found insuline-like growth factor II (IGF II) and its receptor. Whereas IGF II is strongly up-regulated in wt-cells as detected by microarrays and RT-PCR, pbx1-/- cells do not express detectable levels of this growth factor at any ***differentiation*** stage. We have also identified IGF II as a potential E2A-Pbx1 target in NIH3T3 fibroblast systems. Regulation of IGF II by E2A-Pbx1 could be relevant for the molecular pathogenesis of leukemia because IGFII has been implicated to function as B-cell growth promoting factor and in general plays a role in the regulation of hematopoietic cell growth.

L16 ANSWER 14 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:257268 BIOSIS <<LOGINID::20071018>>
DN PREV200300257268
TI Xenopus X-box binding protein 1, a leucine zipper transcription factor, is involved in the ***BMP*** signaling pathway.
AU Zhao, Hui; Cao, Ying; Grunz, Horst [Reprint Author]
CS Department of Zoophysiology, University of Essen, Universitaetsstrasse 5, D-45117, Essen, Germany
h.grunz@uni-essen.de
SO Developmental Biology, (***May 15 2003***) Vol. 257, No. 2, pp. 278-291. print.
ISSN: 0012-1606 (ISSN print).
DT Article
LA English
ED Entered STN: 4 Jun 2003
Last Updated on STN: 4 Jun 2003
AB We describe a novel basic leucine zipper transcription factor, XXBP-1, which interacts with ***BMP*** -4 in a positive feedback loop. It is a maternal factor and is zygotically expressed in the dorsal blastopore lip and ventral ectoderm with the exception of the prospective neural plate during gastrulation. Overexpression of XXBP-1 leads to ventralization of early embryos as described for ***BMP*** -4, and inhibits neuralization of dissociated ectoderm. Consistent with mediating ***BMP*** signaling, we show that the ectopic expression of XXBP-1 recovers the expression of epidermal keratin and reverses the dorsalization imposed by truncated ***BMP*** receptor type I, indicating that it may act downstream of the ***BMP*** receptor. Its effects can be partially mimicked by a ***fusion*** construct containing the VP16 activator domain and the XXBP-1 DNA-binding domain. In contrast, fusing the DNA-binding domain to the even-skipped repressor domain leads to upregulation of the neural markers NCAM and nrp-1 in animal cap assay. Taken together, the results suggest a role for XXBP-1 in the control of neural ***differentiation*** , possibly as an activator.

L16 ANSWER 15 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:106686 BIOSIS <<LOGINID::20071018>>
DN PREV200300106686
TI Dlx proteins position the neural plate border and determine adjacent cell fates.
AU Woda, Juliana M.; Pastagia, Julie; Mercola, Mark [Reprint Author]; Artinger, Kristin Bruk
CS Stem Cell and Regeneration Program, Burnham Institute, 10901 N. Torrey Pines Road, La Jolla, CA, 92037, USA
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SO Development (Cambridge), (***January 2003***) Vol. 130, No. 2, pp. 331-342. print.
CODEN: DEVPED. ISSN: 0950-1991.
DT Article
LA English
ED Entered STN: 26 Feb 2003
Last Updated on STN: 26 Feb 2003
AB The lateral border of the neural plate is a major source of signals that induce primary neurons, neural crest cells and cranial placodes as well as provide patterning cues to mesodermal structures such as somites and heart. Whereas secreted ***BMP*** , FGF and Wnt proteins influence the ***differentiation*** of neural and non-neural ectoderm, we show here that members of the Dlx family of transcription factors position the border between neural and non-neural ectoderm and are required for the specification of adjacent cell fates. Inhibition of endogenous Dlx activity in Xenopus embryos with an EnR-Dlx homeodomain ***fusion*** protein expands the neural plate into non-neural ectoderm tissue whereas ectopic activation of Dlx target genes inhibits neural plate ***differentiation*** . Importantly, the stereotypic pattern of border cell fates in the adjacent ectoderm is re-established only under conditions where the expanded neural plate abuts Dlx-positive non-neural ectoderm. Experiments in which presumptive neural plate was grafted to ventral ectoderm reiterate induction of neural crest and placodal lineages and also demonstrate that Dlx activity is required in non-neural ectoderm for the production of signals needed for induction of these cells. We propose that Dlx proteins regulate intercellular signaling across the interface between neural and non-neural ectoderm that is critical for inducing and patterning adjacent cell fates.

L16 ANSWER 16 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:49062 BIOSIS <<LOGINID::20071018>>
DN PREV200300049062
TI Randomized radiostereometric study comparing osteogenic protein-1 (***BMP*** -7) and autograft bone in human noninstrumented posterolateral lumbar ***fusion*** : 2002 Volvo award in clinical studies.
AU Johnsson, Ragnar [Reprint Author]; Stromqvist, Bjorn; Aspenberg, Per
CS Department of Orthopedics, Lund University Hospital, S-221 85, Lund, Sweden
ragnarjohnsson@spray.se
SO Spine, (***December 1 2002***) Vol. 27, No. 23, pp. 2654-2661. print.
ISSN: 0362-2436 (ISSN print).
DT Article
LA English
ED Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003
AB Study Design: Randomized efficacy trial comparing two types of noninstrumented posterolateral ***fusion*** between L5 and S1 in patients with L5 spondylolysis and vertebral slip less than 50%, as evaluated by radiostereometric analysis. Objective: To determine whether osteogenic protein-1 (***BMP*** -7) in the OP-1 Implant yields better stabilizing bony ***fusion*** than autograft bone. Summary of Background Data: Animal studies of osteoinductive proteins in noninstrumented posterolateral fusions have shown high ***fusion*** rates. No similar conclusive study on humans has been performed. Methods: For this study, 20 patients were randomized to ***fusion*** with either OP-1 Implant or autograft bone from the iliac crest, 10 in each group. The patients were instructed to keep the trunk straight for 5 months after surgery with the aid of a soft lumbar brace. At surgery 0.8-mm metallic markers were positioned in L5 and the sacrum, enabling radiostereometric follow-up analysis during 1 year. The three-dimensional vertebral movements, as measured by radiostereometric analysis induced by positional change from supine posture to standing and sitting, were calculated with an accuracy of 0.5 to 0.7 mm and 0.5degree to 2.0degree. Conventional radiography was added. Results: No significant difference was noted between the radiostereometric and radiographic results of ***fusion*** with the OP-1 Implant and ***fusion*** with autograft bone. There was a significant relation between reduced vertebral movements and better ***bone*** ***formation*** . No adverse effects of the OP-1 Implant occurred. Persistent minor pain at the iliac crest was noticed in one patient. Conclusions: There was no significant difference between the two ***fusion*** versions. Thus, the OP-1 Implant did not yield better stabilizing bony ***fusion*** than autograft bone.

L16 ANSWER 17 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:613948 BIOSIS <<LOGINID::20071018>>
DN PREV200200613948
TI Ex vivo bone morphogenetic protein-9 gene therapy using human mesenchymal
stem cells induces spinal ***fusion*** in rodents.
AU Dumont, Randall J.; Dayoub, Hayan; Li, Jin Zhong; Dumont, Aaron S.; Kallmes, David F.; Hankins, Gerald R.; Helm, Gregory A. [Reprint author]

CS Department of Neurological Surgery, University of Virginia, P.O. Box 800212, Charlottesville, VA, 22908, USA
gah9r@virginia.edu
SO Neurosurgery (Hagerstown), (***November, 2002***) Vol. 51, No. 5, pp. 1239-1245. print.
ISSN: 0148-396X.
DT Article
LA English
ED Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002
AB OBJECTIVE: Ex vivo gene therapy with the use of human mesenchymal stem cells (hMSCs) and bone morphogenetic protein (***BMP***) genes provides a local supply of precursor cells and a supraphysiological dose of osteoinductive molecules that may promote ***bone*** ***formation*** in patients with inadequate hMSC populations because of age, osteoporosis, metastatic bone disease, iatrogenic depletion, or other metabolic derangements. This study was undertaken to evaluate the efficacy of ex vivo gene therapy with the use of hMSCs and the ***BMP*** -9 gene to promote spinal ***fusion*** in the rat. METHODS: Sixteen athymic nude rats were treated with hMSCs transduced with recombinant, replication-defective Type 5 adenovirus containing the cytomegalovirus promoter and either the ***BMP*** -9 (Ad- ***BMP*** -9) or the beta-galactosidase (Ad-beta-gal) gene. Ad-beta-gal served as the control. Each animal received a percutaneous, paraspinal injection of 106 hMSCs transduced with 50 plaque-forming units/cell adenovirus in the lumbar region, with Ad- ***BMP*** -9 on the left and Ad-beta-gal on the right. At 8 weeks postinjection, computed tomographic scans of the lumbosacral spine were obtained, and the lumbosacral spine specimens were examined histologically. RESULTS: Both computed tomographic studies and histological analysis clearly demonstrated large volumes of ectopic bone at the Ad- ***BMP*** -9-transduced hMSC injection sites, resulting in successful spinal ***fusion*** and no evidence of nerve root compression or local or systemic toxicity. The contralateral regions that were treated with Ad-beta-gal-transduced hMSCs showed no evidence of osteogenesis. CONCLUSION: The results of this study suggest that hMSC and ***BMP*** -9 ex vivo gene therapy may be useful in inducing spinal ***fusion*** as well as other related procedures and certainly warrants further clinical development.

L16 ANSWER 18 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:602255 BIOSIS <<LOGINID::20071018>>
DN PREV200200602255
TI Distinct requirements for extra-embryonic and embryonic bone morphogenetic protein 4 in the formation of the node and primitive streak and coordination of left-right asymmetry in the mouse.
AU Fujiwara, Takeshi; Dehart, Deborah B.; Sulik, Kathleen K.; Hogan, Brigid L. M. [Reprint author]
CS Department of Cell Biology, Howard Hughes Medical Institute, Vanderbilt University Medical Center, 1161 21st Ave. South, Nashville, TN, 37232-2175, USA
brigid.hogan@mcmail.vanderbilt.edu
SO Development (Cambridge), (***October, 2002***) Vol. 129, No. 20, pp. 4685-4696. print.
CODEN: DEVPED. ISSN: 0950-1991.
DT Article
LA English
ED Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002
AB In the mouse and chick embryo, the node plays a central role in generating left-right (LR) positional information. Using several ***different*** strategies, we provide evidence in the mouse that bone morphogenetic protein 4 (Bmp4) is required independently in two ***different*** sites for node morphogenesis and for LR patterning. Bmp4 expression in the trophoblast-derived extra-embryonic ectoderm is essential for the normal formation of the node and primitive streak. However, tetraploid ***chimera*** analysis demonstrates that Bmp4 made in epiblast-derived tissues is required for robust LR patterning, even when normal node morphology is restored. In the absence of embryonic Bmp4, the expression of left-side determinants such as Nodal and Lefty2 is absent in the left lateral plate mesoderm (LPM). Noggin-mediated inhibition of ***Bmp*** activity in cultured wild-type embryos results in suppression of Nodal expression in the LPM. Thus, unlike previous models proposed in the chick embryo in which Bmp4 suppresses left-sided gene expression, our results suggest that ***Bmp*** acts as a positive facilitator of the left-sided molecular cascade and is required for Nodal induction and maintenance in the left LPM.

L16 ANSWER 19 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:494865 BIOSIS <<LOGINID::20071018>>
DN PREV200200494865
TI Role of versican in anagen hair induction during hair cycle.
AU Kishimoto, J. [Reprint author]; Soma, T.; Hibino, T. [Reprint author]
CS Hair care laboratories, Shiseido Basic Research Center, Yokohama, Japan
SO Journal of Investigative Dermatology, (***July, 2002***) Vol. 119, No. 1, pp. 287. print.
Meeting Info.: 63rd Annual Meeting of the Society for Investigative Dermatology. Los Angeles, California, USA. May 15-18, 2002.
CODEN: JIDEAE. ISSN: 0022-202X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 18 Sep 2002
Last Updated on STN: 18 Sep 2002

L16 ANSWER 20 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:493826 BIOSIS <<LOGINID::20071018>>
DN PREV200200493826
TI Overview of bone morphogenetic proteins.
AU Wozney, John M. [Reprint author]
CS Wyeth Research, 87 CambridgePark Drive, Cambridge, MA, 02140, USA
jwozney@wyeth.com
SO Spine, (***August 15, 2002***) Vol. 27, No. 16S Supplement, pp. S2-S8. print.
CODEN: SPINDD. ISSN: 0362-2436.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 18 Sep 2002
Last Updated on STN: 18 Sep 2002
AB Study Design: A literature review was conducted. Objectives: To review the discovery of the bone morphogenetic proteins and describe the bone morphogenetic protein products that will or may be available for clinical use. Summary of Background Data: Bone morphogenetic proteins comprise the osteoinductive component of several tissue engineering products in late-stage development as replacements for autogenous bone graft, and for bone augmentation and repair. Methods: The literature on bone morphogenetic proteins was reviewed. Results: Bone morphogenetic proteins were discovered originally on the basis of their presence in osteoinductive extracts of bone matrix. Molecular cloning of bone morphogenetic proteins demonstrated that they are a family of related ***differentiation*** factors, each capable of inducing the formation of new bone tissue when implanted. Two of the molecules in clinical use, recombinant human bone morphogenetic protein-2 and recombinant human bone
morphogenetic protein-7 (OP-1) are produced in a biotechnology process using recombinant deoxyribonucleic acid technology that offers unlimited supply and substantial control over purity and reproducible activity. A third material, bovine bone morphogenetic protein extract, is extracted from bone, and contains a mixture of bone morphogenetic protein molecules. Each of these molecules, although osteoinductive in vivo, has ***different*** physiologic roles and biologic activities in vivo and in vitro. Successful development of a product for use in spinal ***fusion*** involves selecting the osteoinductive molecule, the amount of the bone morphogenetic protein required, and the method of delivery, as well as conducting subsequent preclinical and clinical studies to evaluate its efficacy and safety. Conclusions: On the basis of the data provided in this issue of Spine, some of these bone morphogenetic protein-based products provide for revolutionary therapies in orthopedic practice.

L16 ANSWER 21 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:427779 BIOSIS <<LOGINID::20071018>>
DN PREV200200427779
TI Bone morphogenetic protein-2 application by a poly(D,L-lactide)-coated interbody cage: In vivo results of a new carrier for growth factors.
AU Kandziora, Frank [Reprint author]; Bail, Hermann; Schmidmaier, Gerhard; Schollmeier, Georg; Scholz, Matti; Knispel, Christian; Hiller, Timo; Pflugmacher, Robert; Mittlmeier, Thomas; Raschke, Michael; Haas, Norbert P.
CS Unfall- und Wiederherstellungschirurgie, Universitaetsklinikum Charite, Humboldt Universitaet Berlin, Augustenburgerplatz 1, Campus Virchow Klinikum, 13353, Berlin, Germany
frank.kandziora@charite.de
SO Journal of Neurosurgery, (***July, 2002***) Vol. 97, No. 1 Supplement, pp. 40-48. print.
CODEN: JONSAC. ISSN: 0022-3085.
DT Article
LA English
ED Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002
AB Object. Growth factors such as bone morphogenetic protein-2 (***BMP*** -2) have been proven to promote spine ***fusion*** and to overcome the disadvantages of an autologous bone graft. The optimum method to deliver such growth factors remains a matter of discussion. The purpose of this study was to determine the safety and efficacy of a new poly(D,L-lactide) (PDLLA) carrier system for ***BMP*** -2 and to compare this carrier system with a collagen sponge carrier in a sheep cervical spine interbody ***fusion*** model. Methods. Thirty-two sheep underwent C3-4 discectomy and ***fusion*** : Group 1, titanium cage (eight animals); Group 2, titanium cage coated with a PDLLA carrier (eight animals); Group 3, titanium cage coated with a PDLLA carrier including ***BMP*** -2 (150 mug) (eight animals); and Group 4, titanium cage combined with a collagen sponge carrier including ***BMP*** -2 (150 mug) (eight animals). Blood samples, body weight, and temperature were assessed. Radiographs were obtained pre- and postoperatively and after 1, 2, 4, 8, and 12 weeks. At the same time points, disc space height, intervertebral angle, and lordosis angle were measured. After the sheep were killed 12 weeks postoperatively, flexion-extension radiography was performed to evaluate ***fusion*** sites. Quantitative computerized tomography

scans were obtained to assess bone mineral density (BMD), bone mineral content (BMC), and bone callus volume (BCV). Biomechanical testing was performed in flexion, extension, axial rotation, and lateral bending. Stiffness, range of motion, neutral, and elastic zone were determined. Histomorphological and -morphometrical analyses were performed, and polychrome sequential labeling was used to determine the timeframe of new ***bone*** ***formation*** . There were no differences among the groups concerning blood counts, body weight, and temperature. Compared with the noncoated cages, all PDLLA-coated cages showed significantly higher values for BMD of the callus, as well as slightly higher values for BMC, BCV, and the bone volume/total volume ratio. In comparison with the cage-alone group, the ***BMP*** -2 groups showed significantly higher values for BMD and biomechanical stiffness. Histomorphological, -morphometrical, and polychrome sequential labeling analyses demonstrated greater progression of callus formation in the ***BMP*** -2 groups than in any other group. Compared with ***BMP*** -2 delivered using a collagen sponge carrier, ***BMP*** -2 application with a PDLLA carrier resulted in a higher BCV and a greater progression of interbody callus formation in the histomorphometrical analysis. Conclusions. The use of cervical spine interbody ***fusion*** cages coated with PDLLA as a delivery system for growth factors was effective. In this 12-week follow-up study, the PDLLA coating showed no adverse effects. The slight but not significant positive effect of the PDLLA carrier on interbody ***fusion*** might be a result of the degradation process of the biodegradable carrier. Compared with collagen sponge delivery of ***BMP*** -2, the PDLLA-coated interbody cages significantly increased the results of interbody bone matrix formation. In this new combination (implant + PDLLA + growth factor) the cage represents a "real ***fusion*** " cage, because it not only serves as a mechanical device for spinal fixation but also as a local drug delivery system.

L16 ANSWER 22 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:425638 BIOSIS <<LOGINID::20071018>>
DN PREV200200425638
TI Regulation of human cranial osteoblast phenotype by FGF-2, FGFR-2 and ***BMP*** -2 signaling.
AU Marie, P. J. [Reprint author]; Debiais, F.; Hay, E.
CS Laboratory of Osteoblast Biology and Pathology, INSERM Unite 349 affiliated, Hopital Lariboisiere, 2 rue Ambroise Pare, 75475, Paris Cedex, 10, France
pierre.marie@inserm.lrb.ap-hop-paris.fr
SO Histology and Histopathology, (***July, 2002***) Vol. 17, No. 3, pp. 877-885. print.
ISSN: 0213-3911.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002
AB The formation of cranial bone requires the ***differentiation*** of osteoblasts from undifferentiated mesenchymal cells. The balance between osteoblast recruitment, proliferation, ***differentiation*** and apoptosis in sutures between cranial bones is essential for calvarial ***bone*** ***formation*** . The mechanisms that control human osteoblasts during normal calvarial ***bone*** ***formation*** and premature suture ossification (craniosynostosis) begin to be understood. Our studies of the human calvaria osteoblast phenotype and calvarial ***bone*** ***formation*** showed that premature ***fusion*** of the sutures in non-syndromic and syndromic (Apert syndrome) craniosynostoses results from precocious osteoblast ***differentiation*** . We showed that Fibroblast Growth Factor-2 (FGF-2), FGF receptor-2 (FGFR-2) and Bone Morphogenetic Protein-2 (***BMP*** -2), three essential factors involved in skeletal development, regulate the proliferation, ***differentiation*** and apoptosis in human calvaria osteoblasts. Mechanisms that induce the ***differentiated*** osteoblast phenotype have also been identified in human calvaria osteoblasts. We demonstrated the implication of molecules (N-cadherin, Il-1) and signaling pathways (src, PKC) by which these local factors modulate human calvaria osteoblast ***differentiation*** and apoptosis. The identification of these essential signaling molecules provides new insights into the pathways controlling the ***differentiated*** osteoblast phenotype, and leads to a more comprehensive view in the mechanisms that control normal and premature cranial ossification in humans.

L16 ANSWER 23 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:198983 BIOSIS <<LOGINID::20071018>>
DN PREV200200198983
TI Hematopoietic potential of ex vivo manipulated murine skeletal muscle CD45-Sca-1+c-kit- cells.
AU Howell, Jonathan C. [Reprint author]; Hall, Kristin M. [Reprint author]; Cornetta, Kenneth [Reprint author]; Yoder, Mervin C.; Srour, Edward F. [Reprint author]
CS Microbiology/Immunology, Indiana University School of Medicine, Indianapolis, IN, USA
SO Blood, (***November 16, 2001***) Vol. 98, No. 11 Part 1, pp. 545a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002
AB Pluripotent stem cells (PSC), which are poorly defined in the adult, offer a potentially attractive target for the study of ex vivo conditions that promote the ***differentiation*** of such cells into the hematopoietic lineage. Our laboratory has previously reported that freshly derived and cultured murine skeletal muscle CD45-Sca-1+c-kit- cells support hematopoietic reconstitution in lethally irradiated recipients (Blood 96:11 495a, 2000 abstr). Skeletal muscle cells from the thighs of 4-10 day old C57BL/6 mice were harvested; digested with collagenase I and dispase, and sorted flow cytometrically to yield the CD45-Sca-1+c-kit- population. To examine the in vitro behavior and ***differentiation*** potential of these cells in response to ***different*** stimuli, 5X104 CD45-Sca-1+c-kit- cells were cultured in MEM+10% horse serum in the presence of either no cytokines; 5ng/ml of mSCF, MGDF, and mFlt-3L (3 cytokines); or 5ng/ml of mSCF, MGDF, mFlt-3L, ***BMP*** -4 and mVEGF (5 cytokines). Whereas cultures including no cytokines and 3 cytokines displayed an adherent morphology and expanded 5-6 fold in a low oxygen tension environment after 9 days, cultured cells in the presence of 5 cytokines expanded 8 fold and appeared small and round. To investigate the marrow repopulating potential of the CD45-Sca-1+c-kit- population, 5X104 freshly isolated cells and an equal number from each day 9 expanded culture were transplanted into lethally irradiated B6.BoyJ mice in competitive repopulation assays. At 4 months post-transplant, CD45.1 vs. CD45.2 analysis of recipient peripheral blood revealed that fresh cells displayed 9.7%+-1.2% (n=3) donor-derived ***chimerism*** . Additionally, cells cultured in the presence of 5 cytokines yielded significantly higher donor cell ***chimerism*** (7.22%+-1.9%, n=6) than those cultured with no cytokines (2.62%+-0.3%, n=5) or three cytokines (2.63%+-0.4%, n=5). These data suggest that ***BMP*** -4 and VEGF enhance the hematopoietic ***differentiation*** of cultured CD45-Sca-1+c-kit- cells while allowing the cells to expand ex vivo. To assess the utility of these cells as targets for retroviral-mediated gene transfer, CD45-Sca-1+c-kit- cells cultured in the presence of 5 cytokines were transduced with AM12/eGFP retrovirus overnight in the absence of serum and transplanted into lethally irradiated recipients in competitive repopulation assays (3X104/recipient). GFP+ cells in the peripheral blood at 2 months post-transplant constituted 15.3%+-4.8% (n=3) of donor-derived cells. Furthermore, analysis of recipient peripheral blood for CD4, CD8, B220, GR-1 and Mac-1 expression indicated that 45% of GFP+ cells were lymphoid in origin, and 29% were granulocyte/macrophage in origin demonstrating multilineage ***differentiation*** of transduced cells. These data demonstrate that skeletal muscle-derived PSC can be manipulated ex vivo to retain and perhaps amplify their pluripotent ***differentiation*** capacity and illustrate that these cells may be excellent targets for retroviral-mediated gene transfer.

L16 ANSWER 24 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:53180 BIOSIS <<LOGINID::20071018>>
DN PREV200200053180
TI The N domain of Smad7 is essential for specific inhibition of transforming growth factor-beta signaling.
AU Hanyu, Aki; Ishidou, Yasuhiro; Ebisawa, Takanori; Shimanuki, Tomomasa; Imamura, Takeshi; Miyazono, Kohei [Reprint author]
CS Department of Biochemistry, The JFCR Cancer Institute, 1-37-1 Kami-ikebukuro, Toshima-ku, Tokyo, 170-8455, Japan
miyazono-ind@umin.ac.jp
SO Journal of Cell Biology, (***December 10, 2001***) Vol. 155, No. 6, pp. 1017-1027. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DT Article
LA English
ED Entered STN: 9 Jan 2002
Last Updated on STN: 25 Feb 2002
AB Inhibitory Smads (I-Smads) repress signaling by cytokines of the transforming growth factor-beta (TGF-beta) superfamily. I-Smads have conserved carboxy-terminal Mad homology 2 (MH2) domains, whereas the amino acid sequences of their amino-terminal regions (N domains) are highly divergent from those of other Smads. Of the two ***different*** I-Smads in mammals, Smad7 inhibited signaling by both TGF-beta and bone morphogenetic proteins (BMPs), whereas Smad6 was less effective in inhibiting TGF-beta signaling. Analyses using deletion mutants and ***chimeras*** of Smad6 and Smad7 revealed that the MH2 domains were responsible for the inhibition of both TGF-beta and ***BMP*** signaling by I-Smads, but the isolated MH2 domains of Smad6 and Smad7 were less potent than the full-length Smad7 in inhibiting TGF-beta signaling. The N domains of I-Smads determined the subcellular localization of these molecules. ***Chimeras*** containing the N domain of Smad7 interacted with the TGF-beta type I receptor (TbetaR-I) more efficiently, and were more potent in repressing TGF-beta signaling, than those containing the N domain of Smad6. The isolated N domain of Smad7 physically interacted with the MH2 domain of Smad7, and enhanced the inhibitory activity of the latter through facilitating interaction with TGF-beta receptors. The N domain of Smad7 thus plays an important role in the specific inhibition of

TGF-beta signaling.

L16 ANSWER 25 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:573250 BIOSIS <<LOGINID::20071018>>
DN PREV200100573250
TI The transcription function of Dlx5 is regulated by a RING-finger protein praja-1 through ubiquitin-dependent degradation of Dlxin-1, a Dlx/Msx-interacting protein.
AU Sasaki, A. [Reprint author]; Ikeda, K. [Reprint author]; Watanabe, K. [Reprint author]
CS Dept of Geriatric Res, Natl Inst for Longevity Sci, Obu, Japan
SO Journal of Bone and Mineral Research, (***September, 2001***) Vol. 16, No. Suppl. 1, pp. S367. print.
Meeting Info.: Twenty-Third Annual Meeting of the American Society for Bone and Mineral Research. Phoenix, Arizona, USA. October 12-16, 2001.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 12 Dec 2001
Last Updated on STN: 25 Feb 2002

L16 ANSWER 26 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:558457 BIOSIS <<LOGINID::20071018>>
DN PREV200100558457
TI Xiro-1 controls mesoderm patterning by repressing ***bmp*** -4 expression in the Spemann organizer.
AU Glavic, Alvaro; Gomez-Skarmeta, Jose Luis; Mayor, Roberto [Reprint author]
CS Millennium Nucleus in Developmental Biology, Laboratory of Developmental Biology, Faculty of Science, University of Chile, Casilla 653, Santiago, Chile
rmayor@abello.dic.uchile.cl
SO Developmental Dynamics, (***November, 2001***) Vol. 222, No. 3, pp. 368-376. print.
CODEN: DEDYEI. ISSN: 1058-8388.
DT Article
LA English
ED Entered STN: 5 Dec 2001
Last Updated on STN: 25 Feb 2002
AB The Iroquois genes code for homeodomain proteins that have been implicated in the neural development of Drosophila and vertebrates. We show here for the first time that Xiro-1, one of the Xenopus Iroquois genes, is expressed in the Spemann organizer from the start of gastrulation and that its overexpression induces a secondary axis as well as the ectopic expression of several organizer genes, such as chordin, goosecoid, and Xlim-1. Our results also indicate that Xiro-1 normally functions as a transcriptional repressor in the mesoderm. Overexpression of Xiro-1 or a ***chimeric*** form fused to the repressor domain of Engrailed cause similar phenotypes while overexpression of functional derivatives of Xiro-1 fused with transactivation domains (VP16 or E1A) produce the opposite effects. Finally, we show that Xiro-1 works as a repressor of ***bmp*** -4 transcription and that its effect on organizer development is dependent on ***BMP*** -4 activity. We propose that the previously observed down regulation of ***bmp*** -4 in the dorsal mesoderm during gastrulation can be explained by the repressor activity of Xiro-1 described here. Thus, Xiro-1 seems to have at least two ***different*** functions: control of neural plate and organizer development, both of which could be mediated by repression of ***bmp*** -4 transcription.

L16 ANSWER 27 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:523322 BIOSIS <<LOGINID::20071018>>
DN PREV200100523322
TI 16S rRNA-targeted identification of cyanobacterial genera using oligonucleotide-probes immobilized on bacterial magnetic particles.
AU Matsunaga, Tadashi [Reprint author]; Takeyama, Haruko; Nakayama, Hideki
CS Department of Biotechnology, Tokyo University of Agriculture and Technology, 2-24-16 Naka-Cho, Koganei, Tokyo, 184-8588, Japan
tmatsuna@cc.tuat.ac.jp
SO Journal of Applied Phycology, (***August, 2001***) Vol. 13, No. 4, pp. 389-394. print.
CODEN: JAPPEL. ISSN: 0921-8971.
DT Article
LA English
ED Entered STN: 7 Nov 2001
Last Updated on STN: 23 Feb 2002
AB 16S rRNA-targeted identification of cyanobacterial genera, Anabaena, Microcystis, Nostoc, Oscillatoria, Synechococcus was developed using bacterial magnetic particles (BMPs). 16S rRNA-targeted capture probes designed from the genus specific region of the 16S rRNA sequence were immobilized on BMPs. Identification of cyanobacteria was performed by a sandwich hybridization using the capture probes - ***BMP*** ***conjugates*** and a digoxigenin (DIG)-labeled detector probe complementary to the highly conserved 16S rRNA sequence for cyanobacteria. The luminescence intensity of the probe/target- ***BMP*** hybrids was measured after reaction with alkaline phosphatase ***conjugated*** anti-DIG antibody. Five species of cyanobacteria from five ***different*** genera were successfully discriminated using this magnetic capture system.

L16 ANSWER 28 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:492689 BIOSIS <<LOGINID::20071018>>
DN PREV200100492689
TI Neptune, a Kruppel-like transcription factor that participates in primitive erythropoiesis in Xenopus.
AU Huber, Tara L.; Perkins, Andrew C.; Deconinck, Anne E.; Chan, Fung Yee; Mead, Paul E.; Zon, Leonard I. [Reprint author]
CS Division of Hematology/Oncology, Children's Hospital, Harvard Medical School, Boston, MA, 02115, USA
zon@genetics.med.harvard.edu
SO Current Biology, (***18 September, 2001***) Vol. 11, No. 18, pp. 1456-1461. print.
CODEN: CUBLE2. ISSN: 0960-9822.
DT Article
LA English
ED Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002
AB The specification of the erythroid lineage from hematopoietic stem cells requires the expression and activity of lineage-specific transcription factors. One transcription factor family that has several members involved in hematopoiesis is the Kruppel-like factor (KLF) family. For example, erythroid KLF (EKLF) regulates beta-globin expression during erythroid ***differentiation*** . KLFs share a highly conserved zinc finger-based DNA binding domain (DBD) that mediates binding to CACCC-box and GC-rich sites, both of which are frequently found in the promoters of hematopoietic genes. Here, we identified a novel Xenopus KLF gene, neptune, which is highly expressed in the ventral blood island (VBI), cranial ganglia, and hatching and cement glands. neptune expression is induced in response to components of the ***BMP*** -4 signaling pathway in injected animal cap explants. Similar to its family member, EKLF, Neptune can bind CACCC-box and GC-rich DNA elements. We show that Neptune
cooperates with the hematopoietic transcription factor XGATA-1 to enhance globin induction in animal cap explants. A ***fusion*** protein comprised of Neptune's DBD and the Drosophila engrailed repressor domain suppresses the induction of globin in ventral marginal zones and in animal caps. These studies demonstrate that Neptune is a positive regulator of primitive erythropoiesis in Xenopus.

L16 ANSWER 29 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:483265 BIOSIS <<LOGINID::20071018>>
DN PREV200100483265
TI Characterization of the DNA-binding property of Smad5.
AU Li, Wei; Chen, Feifei; Nagarajan, Raman P.; Liu, Xubao; Chen, Yan [Reprint author]
CS Department of Medical and Molecular Genetics, Indiana University School of Medicine, 975 West Walnut Street IB130, Indianapolis, IN, 46202, USA
ychen3@iupui.edu
SO Biochemical and Biophysical Research Communications, (***September 7,*** *** 2001***) Vol. 286, No. 5, pp. 1163-1169. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 17 Oct 2001
Last Updated on STN: 23 Feb 2002
AB Activation of TGF-beta superfamily receptors leads to phosphorylation of Smad proteins which function as transcription factors to regulate gene expression. Previous studies have indicated that Smad5, together with Smad1 and Smad8, participates in signaling downstream of ***BMP*** receptors. To characterize the DNA-binding characteristics of Smad5, we used the GST-Smad5 N-terminal ***fusion*** protein to select for random oligonucleotide sequences that were able to binds the protein. As a result, we found that Smad5 is able to bind a consensus sequence TGTGC. We further used the Smad7 promoter sequence that contains a Smad-binding element (SBE), GTCTAGAC to determine how mutations in each nucleotide in the SBE affects the binding with Smad5, compared with the binding with Smad1, Smad2, Smad3, Smad4, and Smad8. Interestingly, Smad5, but not Smad1 and Smad8, was able to bind the SBE, at a level similar to the binding by Smad3 and Smad4. However, mutations at the SBE had ***different*** effect on the binding with Smad5, compared to that with Smad3 and Smad4. These studies suggest that even though Smad5 falls into the same subfamily with Smad1 and Smad8 in mediating the signaling by ***BMP*** receptors, it has an unique DNA-binding property that is similar to Smad3, which specifically transduces signaling for TGF-beta and activin receptors.

L16 ANSWER 30 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:440847 BIOSIS <<LOGINID::20071018>>
DN PREV200100440847
TI The cytoplasmic amino-terminus of the Latent Membrane Protein-1 of Epstein-Barr virus: Relationship between transmembrane orientation and effector functions of the carboxy-terminus and transmembrane domain.
AU Coffin, William F., III; Erickson, Kimberly D.; Hoedt-Miller, Marloes; Martin, Jennifer M. [Reprint author]

CS Department of Molecular, Cellular, and Developmental Biology, University of Colorado, Boulder, CO, 80309, USA
jm@stripe.colorado.edu
SO Oncogene, (***30 August, 2001***) Vol. 20, No. 38, pp. 5313-5330. print.
CODEN: ONCNES. ISSN: 0950-9232.
DT Article
LA English
ED Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002
AB The Latent Membrane Protein 1 (***LMP*** - ***1***) protein of Epstein-Barr virus (EBV) is localized in the plasma membrane of the infected cell. ***LMP*** - ***1*** possesses a hydrophobic membrane spanning domain, and charged, intracellular amino- and carboxy-termini. Two models have been proposed for the contribution of the amino-terminus to ***LMP*** - ***1*** 's function: (i) as an effector domain, interacting with cellular proteins, or (ii) as a structural domain dictating the correct orientation of transmembrane domains and thereby positioning ***LMP*** - ***1*** 's critical effector domains (i.e. the carboxy-terminus). However, no studies to date have addressed directly the structural contributions of ***LMP*** - ***1*** 's cytoplasmic amino-terminus to function. This study was designed to determine if ***LMP*** - ***1*** 's.cytoplasmic amino-terminus (N-terminus) encodes information required solely for maintenance of proper topological orientation. We have constructed ***LMP*** - ***1*** ***chimeras*** in which the cytoplasmic N-terminus of ***LMP*** - ***1*** is replaced with an unrelated domain of similar size and charge, but of ***different*** primary sequence. Retention of the charged amino-terminal (N-terminal) cytoplasmic domain and first predicted transmembrane domain was required for correct transmembrane topology. The absolute primary sequence of the cytoplasmic N-terminus was not critical for ***LMP*** - ***1*** 's cytoskeletal association, turnover, plasma membrane patching, oligomerization, Tumor Necrosis Factor Receptor-associated factor (TRAF) binding, NF-kappaB activation, rodent cell transformation and cytostatic activity. Furthermore, our results point to the hydrophobic transmembrane domain, independent of the cytoplasmic domains, as the primary ***LMP*** - ***1*** domain mediating oligomerization, patching and cytoskeletal association. The cytoplasmic amino-terminus provides the structural information whereby proper transmembrane orientation is achieved.

L16 ANSWER 31 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2001:402998 BIOSIS <<LOGINID::20071018>>
DN PREV200100402998
TI Effect of molecular weight of thermoreversible polymer on in vivo retention of rhBMP-2.
AU Gao, Tiejun [Reprint author]; Uludag, Hasan
CS Department of Biomedical Engineering, Faculty of Medicine, University of Alberta, 1098 RTF Building, Edmonton, AB, T6G 2V2, Canada
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SO Journal of Biomedical Materials Research, (***October, 2001***) Vol. 57, No. 1, pp. 92-100. print.
CODEN: JBMRBG. ISSN: 0021-9304.
DT Article
LA English
ED Entered STN: 22 Aug 2001
Last Updated on STN: 22 Feb 2002
AB To investigate the effect of polymer molecular weight (MW) on rhBMP-2 delivery by thermoreversible polymers, four polymers with similar lower critical solution temperatures (20degree-22degreeC) but ***different*** MWs were studied. Thermoreversible polymers were based on N-isopropylacrylamide (NiPAM), ethyl methacrylate (EMA), and N-acryloxysuccinimide (NASI), and had MWs of either apprx49 kDa or apprx400 kDa. The NASI content was either 0 or 1-1.6%. High MW polymers, irrespective of their NASI content, formed a stable gel with significantly lower water uptake and exhibited a dense micelle with average pore size smaller than the low MW polymers. NiPAM/EMA polymers without NASI did not ***conjugate*** with recombinant human bone morphogenetic protein-2 (rhBMP-2). NiPAM/EMA polymers containing NASI, however, gave ***conjugation*** with rh- ***BMP*** -2. For polymers without NASI, a high MW was essential for rhBMP-2 retention when injected intramuscularly in Sprague-Dawley rats. For NASI-containing polymers, the MW of the polymer did not make a significant difference because rhBMP-2 retention was equivalent for ***different*** size polymers. We conclude that polymer MW affects rhBMP-2 retention in vivo in polymers designed for physical entrapment of rhBMP-2, but not in polymers designed for chemical ***conjugation*** with rhBMP-2.

L16 ANSWER 32 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2001:386434 BIOSIS <<LOGINID::20071018>>
DN PREV200100386434
TI Regulation of limb patterning by extracellular microfibrils.
AU Arteaga-Solis, Emilio; Gayraud, Barbara; Lee, Sui Y.; Shum, Lillian; Sakai, Lynn; Ramirez, Francesco [Reprint author]
CS Department of Biochemistry and Molecular Biology, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY, 10029, USA
ramirf01@doc.mssm.edu
SO Journal of Cell Biology, (***July 23, 2001***) Vol. 154, No. 2, pp. 275-281. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DT Article
LA English
ED Entered STN: 15 Aug 2001
Last Updated on STN: 19 Feb 2002
AB To elucidate the contribution of the extracellular microfibril-elastic fiber network to vertebrate organogenesis, we generated fibrillin 2 (Fbn2)-null mice by gene targeting and identified a limb-patterning defect in the form of bilateral syndactyly. Digit ***fusion*** involves both soft and hard tissues, and is associated with reduced apoptosis at affected sites. Two lines of evidence suggest that syndactily is primarily due to defective mesenchyme ***differentiation*** , rather than reduced apoptosis of interdigital tissue. First, ***fusion*** occurs before appearance of interdigital cell death; second, interdigital tissues having incomplete separation fail to respond to apoptotic clues from implanted ***BMP*** -4 beads. Syndactyly is associated with a disorganized matrix, but with normal ***BMP*** gene expression. On the other hand, mice double heterozygous for null Fbn2 and Bmp7 alleles display the combined digit phenotype of both nullizygotes. Together, these results imply functional interaction between Fbn2-rich microfibrils and ***BMP*** -7 signaling. As such, they uncover an unexpected relationship between the insoluble matrix and soluble factors during limb patterning. We also demonstrate that the Fbn2-null mutation is allelic to the recessive shaker-with-syndactyly (sy) locus on chromosome 18.

L16 ANSWER 33 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2001:334811 BIOSIS <<LOGINID::20071018>>
DN PREV200100334811
TI Effects of the NIK aly mutation on NF-kappaB activation by the Epstein-Barr virus latent infection membrane protein, lymphotoxin beta receptor, and CD40.
AU Luftig, Micah A.; Cahir-McFarland, Ellen; Mosialos, George; Kieff, Elliott [Reprint author]
CS Departments of Microbiology and Molecular Genetics and Medicine, Program in Virology, Harvard Medical School, Boston, MA, 02115, USA
ekieff@rics.bwh.harvard.edu
SO Journal of Biological Chemistry, (***May 4, 2001***) Vol. 276, No. 18, pp. 14602-14606. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 18 Jul 2001
Last Updated on STN: 19 Feb 2002
AB Homozygosity for the aly point mutation in NF-kappaB-inducing kinase (NIK) results in alymphoplasia in mice, a phenotype similar to that of homozygosity for deletion of the lymphotoxin beta receptor (LTbetaR). We now find that NF-kappaB activation by Epstein-Barr virus latent membrane protein 1 (***LMP1***) or by an ***LMP1*** transmembrane domain ***chimera*** with the LTbetaR signaling domain in human embryonic kidney 293 cells is selectively inhibited by a wild type dominant negative NIK comprised of amino acids 624-947 (DN-NIK) and not by aly DN-NIK. In contrast, ***LMP1*** /CD40 is inhibited by both wild type (wt) and aly DN-NIK. ***LMP1*** , an ***LMP1*** transmembrane domain ***chimera*** with the LTbetaR signaling domain, and ***LMP1*** /CD40 activate NF-kappaB in wt or aly murine embryo fibroblasts. Although wt and aly NIK do not differ in their in vitro binding to tumor necrosis factor receptor-associated factor 1, 2, 3, or 6 or in their in vivo association with tumor necrosis factor receptor-associated factor 2 and differ marginally in their very poor binding to IkappaB kinase beta (IKKbeta), only wt NIK is able to bind to IKKalpha. These data are compatible with a model in which activation of NF-kappaB by ***LMP1*** and LTbetaR is mediated by an interaction of NIK or a NIK-like kinase with IKKalpha that is abrogated by the aly mutation. On the other hand, CD40 mediates NF-kappaB activation through a kinase that interacts with a ***different*** component of the IKK complex.

L16 ANSWER 34 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2001:299993 BIOSIS <<LOGINID::20071018>>
DN PREV200100299993
TI Bone morphogenetic proteins expression in acute promyelocytic leukemia correlates with molecular remission.
AU Kusec, R. [Reprint author]; Grcevic, D.; Marusic, A.; Grahovac, B.; Popovic-Bingulac, J.; Vrhovac, R.; Minigo, H.; Jaksic, B.
CS Molecular Medicine, Institute "Rudjer Boskovic", Zagreb, Croatia
SO Blood, (***November 16, 2000***) Vol. 96, No. 11 Part 2, pp. 192b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 20 Jun 2001
Last Updated on STN: 19 Feb 2002
AB Bone morphogenetic proteins (BMPs) belong to TGFbeta superfamily of cytokines with important regulatory roles in embryonic morphogenesis and development, cell growth and ***differentiation*** in various cell types including hematopoietic tissue. Recent studies using RNase

protection assay found increased levels of gene expression for several BMPs in a panel of lymphatic leukemic cell lines. Low levels of BMP2 and 4 expression were seen in normal bone marrow. In the present study we investigated the expression of BMPs and ***BMP*** receptors in human leukemic bone marrow. A model of acute promyelocytic leukemia (APL) was selected. An RT-PCR assay was designed to detect the transcripts of BMP2, 4 and 7 as well the ***BMP*** receptors I, IA, and II before and after leukemia treatment with the ***differentiating*** agent All-trans retinoic acid (ATRA) in combination with chemotherapy. RNA was extracted after minimal manipulation from the bone marrow of four patients at diagnosis and at the points of hematological marrow evaluation as required by the treatment protocol. ***BMP*** 2, 4, and 7 were expressed in the leukemic marrow but they were undetectable in molecularly confirmed remission marrows (maximal sensitivity of the assay 1X10-5). Morphological response with the reduction of pathological cells but without molecular clearance was not sufficient. There was a clear correlation between the BMPs expression and expression of oncogenic ***fusion*** gene transcript PML-RARalpha. When the minimal residual disease was detectable BMPs were expressed too. ***BMP*** receptors expression could be detected in the marrows at all test points irrespective of the disease phase. A research into the nature and cause of the relation of BMPs to the oncogene and the evaluation of BMPs as possible minimal residual disease marker is needed.

L16 ANSWER 35 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2001:286923 BIOSIS <<LOGINID::20071018>>

DN PREV200100286923

TI Synergistic roles of bone morphogenetic protein 15 and growth ***differentiation*** factor 9 in ovarian function.

AU Yan, Changning; Wang, Pei; DeMayo, Janet; DeMayo, Francesco J.; Elvin, Julia A.; Carino, Cecilia; Prasad, Sarvamangala V.; Skinner, Sheri S.; Dunbar, Bonnie S.; Dube, Jennifer L.; Celeste, Anthony J.; Matzuk, Martin M. [Reprint author]

CS Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX, 77030, USA
mmatzuk@bcm.tmc.edu

SO Molecular Endocrinology, (***June, 2001***) Vol. 15, No. 6, pp. 854-866. print.
CODEN: MOENEN. ISSN: 0888-8809.

DT Article

LA English

ED Entered STN: 13 Jun 2001
Last Updated on STN: 19 Feb 2002

AB Knockout mouse technology has been used over the last decade to define the essential roles of ovarian-expressed genes and uncover genetic interactions. In particular, we have used this technology to study the function of multiple members of the transforming growth factor-beta superfamily including inhibins, activins, and growth ***differentiation*** factor 9 (GDF-9 or Gdf9). Knockout mice lacking GDF-9 are infertile due to a block in folliculogenesis at the primary follicle stage. In addition, recombinant GDF-9 regulates multiple cumulus granulosa cell functions in the periovulatory period including hyaluronic acid synthesis and cumulus expansion. We have also cloned an oocyte-specific homolog of GDF-9 from mice and humans, which is termed bone morphogenetic protein 15 (***BMP*** -15 or Bmp15). To define the function of ***BMP*** -15 in mice, we generated embryonic stem calls and knockout mice, which have a null mutation in this X-linked gene. Male ***chimeric*** and Bmp15 null mice are normal and fertile. In contrast to Bmp15 null males and Gdf9 knockout females, Bmp15 null females (Bmp15-/-) are subfertile and usually have minimal ovarian histopathological defects, but demonstrate decreased ovulation and fertilization rates. To further decipher possible direct or indirect genetic interactions between GDF-9 and ***BMP*** -15, we have generated double mutant mice lacking one or both alleles of these related homologs. Double homozygote females (Bmp15-/-Gdf9-/-) display oocyte loss and cysts and resemble Gdf9-/- mutants. In contrast, Bmp15-/-Gdf9+/- female mice have more severe fertility defects than Bmp15-/- females, which appear to be due to abnormalities in ovarian folliculogenesis, cumulus cell physiology, and fertilization. Thus, the dosage of intact Bmp15 and Gdf9 alleles directly influences the destiny of the oocyte during folliculogenesis and in the periovulatory period. These studies have important implications for human fertility control and the maintenance of fertility and normal ovarian physiology.

L16 ANSWER 36 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2001:251413 BIOSIS <<LOGINID::20071018>>

DN PREV200100251413

TI Evaluation of carriers of bone morphogenetic protein for spinal ***fusion*** .

AU Minamide, Akihito [Reprint author]; Kawakami, Mamoru; Hashizume, Hiroshi; Sakata, Ryosuke; Tamaki, Tetsuya

CS Department of Orthopaedic Surgery, Wakayama Medical College, 811-1, Kimiidera, Wakayama City, Wakayama, 641-8510, Japan
minamide@wakayama-med.ac.jp

SO Spine, (***April 15, 2001***) Vol. 26, No. 8, pp. 933-939. print.
CODEN: SPINDD. ISSN: 0362-2436.

DT Article

LA English

ED Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002

AB Study Design: Posterolateral lumbar transverse process ***fusion*** in a rabbit model was performed using two ***different*** carriers for recombinant human morphogenetic protein-2, one having a porous structure and the other being a Type I collagen sheet. Objectives: To compare the effectiveness of two ***different*** carriers for recombinant human morphogenetic protein-2 in achieving lumbar intertransverse process arthrodesis. Summary of Background Data: The application of osteoinductive growth factors at various anatomic sites, such as in long bones and spinal segments, has been performed experimentally by many researchers. Although many carriers of osteoinductive factors have been reported, the most effective carrier has not been established. We have reported the efficacy of sintered bovine bone, True Bone Ceramics, which is coated with Type I collagen as a carrier of recombinant human bone morphogenetic protein-2 in achieving lumbar intertransverse process arthrodesis. True Bone Ceramics is a crystallized form of bone minerals made from sintering bovine bone at high temperatures and possesses natural trabecular structure. The crystalline character of True Bone Ceramics is similar to that of artificial hydroxyapatite. In this study we focused on the structure of two ***different*** carriers to facilitate osteosynthesis in lumbar arthrodesis. Methods: Fifty-four adult rabbits underwent bilateral lumbar intertransverse process arthrodesis at L4-L5. The animals were divided into five groups and had implants placed as follows: Group 1, autograft group, harvested autologous corticocancellous bone from the posterior iliac crest; Group 2, TBC group, True Bone Ceramics alone; Group 3, TBC-TBMP group, True Bone Ceramics coated with Type I collagen infiltrated with 100 mug of recombinant human bone morphogenetic protein-2; Group 4, collagen group, Type I collagen sheet; and Group 5, collagen- ***BMP*** group, implanted collagen sheet containing 100 mug of recombinant human bone morphogenetic protein-2. Spinal ***fusion*** was evaluated by radiographic analysis, manual palpation, biomechanical testing, and histologic examination at both 3 and 6 weeks after surgery. Results: Radiographs in the TBC-TBMP group showed a continuous trabecular pattern within the intertransverse area at 3 weeks after surgery. The ***fusion*** mass in the intertransverse area was more prominent than in the other groups. At 3 weeks after surgery the TBC-TBMP group had higher ***fusion*** rates based on manual palpation, and the fusions showed significantly higher tensile strength and stiffness. The histologic findings in the TBC-TBMP group at 3 weeks after surgery showed a cortical bone rim around the edge of the ***fusion*** mass, and contiguous new bone appearing between the recipient bone and the matrix of TBC without evidence of foreign body formation. In the collagen- ***BMP*** group, less mature ***bone*** ***formation*** was present within the grafted area and the new bone was not contiguous, even at 6 weeks after surgery. Conclusions: As a carrier for recombinant human bone morphogenetic protein-2, True Bone Ceramics, possessing a bony or porous structure, was more effective than a Type I collagen sheet in achieving a faster and stronger lumbar spinal ***fusion*** in a rabbit model.

L16 ANSWER 37 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2001:186087 BIOSIS <<LOGINID::20071018>>

DN PREV200100186087

TI Identification of the ligand-binding site of the ***BMP*** type IA receptor for ***BMP*** -4.

AU Hatta, Tomohisa; Konishi, Hiroko; Katoh, Etsuko; Natsume, Tohru; Ueno, Naoto; Kobayashi, Yuji; Yamazaki, Toshimasa [Reprint author]

CS Structural Biology Unit, National Institute of Agrobiological Resources, Tsukuba, Ibaraki, 305-8602, Japan
yujik@protien.osaka-u.ac.jp; tyamazak@abr.affrc.go.jp

SO Biopolymers, (***2000***) Vol. 55, No. 5, pp. 399-406. print.
CODEN: BIPMAA. ISSN: 0006-3525.

DT Article

LA English

ED Entered STN: 20 Apr 2001
Last Updated on STN: 18 Feb 2002

AB Bone morphogenetic proteins (BMPs) belong to the transforming growth factor-beta (TGF-beta) superfamily of multifunctional cytokines. ***BMP*** induces its signal to regulate growth, ***differentiation*** , and apoptosis of various cells upon trimeric complex formation with two distinct type I and type II receptors on the cell surface: both are single-transmembrane serine/threonine kinase receptors. To identify the amino acid residues on ***BMP*** type I receptor responsible for its ligand binding, the structure-activity relationship of the extracellular ligand-binding domain of the ***BMP*** type IA receptor (sBMPR-IA) was investigated by alanine-scanning mutagenesis. The mutant receptors, as well as sBMPR-IA, were expressed as ***fusion*** proteins with thioredoxin in Escherichia coli, and purified using reverse phase high performance liquid chromatography (RP-HPLC) after digestion with enterokinase. Structural analysis of the parent protein and representative mutants in solution by CD showed no detectable differences in their folding structures. The binding affinity of the mutants to ***BMP*** -4 was determined by surface plasmon resonance biosensor. All the mutant receptors examined, with the exception of Y70A, displayed reduced affinities to ***BMP*** -4 with the rank order of decreases: I52A (17-fold) apprxeq F75A (15-fold) mchgt T64A (4-fold) = T62A (4-fold) apprxeq E54A (3-fold). The decreases in binding affinity observed for the latter three mutants are mainly due to decreased association rate constants while alterations in rate constants both, for association and dissociation, result in the drastically reduced affinities for the former two mutants. These results allow us to conclude that sBMPR-IA recognizes

the ligand using the concave face of the molecule. The major ligand-binding site of the ***BMP*** type IA receptor consists of Phe75 in loop 2 and Ile52, Glu54, Thr62 and Thr64 on the three-stranded beta-sheet. These findings should provide a general basis for the ligand/type I receptor recognition in the TGF-beta superfamily.

L16 ANSWER 38 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:142246 BIOSIS <<LOGINID::20071018>>
DN PREV200100142246
TI Bone morphogenetic protein function is required for terminal ***differentiation*** of the heart but not for early expression of cardiac marker genes.
AU Walters, Melinda J.; Wayman, Gary A.; Christian, Jan L. [Reprint author]
CS Department of Cell and Developmental Biology, School of Medicine, Oregon Health Sciences University, 3181 SW Sam Jackson Park Road, Portland, OR, 97201-3098, USA
christia@ohsu.edu
SO Mechanisms of Development, (***February, 2001***) Vol. 100, No. 2, pp. 263-273. print.
CODEN: MEDVE6. ISSN: 0925-4773.
DT Article
LA English
ED Entered STN: 21 Mar 2001
Last Updated on STN: 15 Feb 2002
AB To examine potential roles for bone morphogenetic proteins (BMPs) in cardiogenesis, we used intracellular ***BMP*** inhibitors to disrupt this signaling cascade in Xenopus embryos. ***BMP*** -deficient embryos showed endodermal defects, a reduction in cardiac muscle-specific gene expression, a decrease in the number of cardiomyoctes and cardia bifida. Early expression of markers of endodermal and precardiac fate, however, was not perturbed. Heart defects were observed even when ***BMP*** signal transduction was blocked only in cells that contribute primarily to endodermal, and not cardiac fates, suggesting a non-cell autonomous function. Our results suggest that BMPs are not required for expression of early transcriptional regulators of cardiac fate but are essential for migration and/or ***fusion*** of the heart primordia and cardiomyocyte ***differentiation*** .

L16 ANSWER 39 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:59288 BIOSIS <<LOGINID::20071018>>
DN PREV200100059288
TI An Epstein-Barr virus protein interacts with Notch.
AU Kusano, Shuichi; Raab-Traub, Nancy [Reprint author]
CS Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, 27599-7295, USA
nrt@med.unc.edu
SO Journal of Virology, (***January, 2001***) Vol. 75, No. 1, pp. 384-395. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
ED Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002
AB The Epstein-Barr virus (EBV) BamHI A mRNAs were originally identified in cDNA libraries from nasopharyngeal carcinoma, where they are expressed at high levels. The RNAs are ***differentially*** spliced to form several open reading frames and also contain the BARF0 open reading frame at the 3' end. One cDNA, RKBARF0, included a potential endoplasmic reticulum-targeting signal peptide sequence. The RK-BARF0 protein is shown here to interact with the Notch4 ligand binding domain, using yeast two- ***hybrid*** screening, coimmunoprecipitation, and confocal microscopy. This interaction induces translocation of a portion of the full-length unprocessed Notch4 to the nucleus by using the Notch nuclear localization signal. These effects of RK-BARF0 on Notch intracellular location indicate that EBV possibly modulates Notch signaling. Unprocessed Notch4 was also detected in immunoprecipitated complexes from EBV-infected cells by using a rabbit antiserum raised against a BARF0-specific peptide. This finding provides additional evidence for expression of RK-BARF0 and its interaction with Notch during EBV infection. In EBV-infected, EBNA2-negative cells, RK-BARF0 induced the expression of EBV latent membrane protein 1 (***LMP1***), and this induction was dependent on the RK-BARF0/Notch interaction domain. The activation of ***LMP1*** expression by RK-BARF0 may be responsible for expression of ***LMP1*** in EBV latent infections in the absence of EBNA2.

L16 ANSWER 40 OF 167 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2000:540971 BIOSIS <<LOGINID::20071018>>
DN PREV200000540971
TI The effect of nicotine on gene expression during spine ***fusion*** .
AU Theiss, Steven M. [Reprint author]; Boden, Scott D.; Hair, Gregory; Titus, Louisa; Morone, Michael A.; Ugbo, John
CS University of Alabama at Birmingham, 1813 Sixth Avenue South, MEB 507, Birmingham, AL, 35294: Steven.Theiss@ortho.uab.edu, USA
SO Spine, (***October 15, 2000***) Vol. 25, No. 20, pp. 2588-2594. print.
CODEN: SPINDD. ISSN: 0362-2436.
DT Article
LA English
ED Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002
AB Study Design: A rabbit model of posterolateral spine ***fusion*** was used to investigate the effect of nicotine on cytokine expression during spine ***fusion*** . Objectives: To determine the effects of nicotine on the known gene expression pattern of bone morphogens and related proteins expressed during spine ***fusion*** . Summary of Background Data: The mechanism by which nicotine increases the pseudarthrosis rate of spine ***fusion*** is unknown. Recently, a distinct temporal and spatial pattern of cytokine expression during ***bone*** ***formation*** has been described. The authors hypothesized that nicotine would alter this known pattern, thereby revealing the mechanism by which nicotine exerts its effect. Methods: Twenty-eight New Zealand White rabbits underwent posterolateral spine ***fusion*** with autogenous bone graft. Fourteen rabbits received systemic nicotine by a miniosmotic pump. Fusions were harvested at 0, 2, 5, and 7 days and 2, 3, and 4 weeks after arthrodesis. Specimens were divided into the outer zones adjacent to the transverse processes and the central zones between the transverse processes. Gene expression of type I and II collagen, bone morphogenic protein-2, -4, and -6 and basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) was then measured at each time point in each of the two zones. Results: Nicotine inhibited expression of all cytokines measured, mainly in the central zone. However, the previously described temporal and spatial patterns of expression were preserved. Conclusions: Nicotine inhibits expression of a wide range of cytokines, including those associated with neovascularization and osteoblast ***differentiation*** . Therefore, the effects of nicotine appear to involve more than just local vasoconstriction.

=> d his

(FILE 'HOME' ENTERED AT 19:29:36 ON 18 OCT 2007)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 19:32:46 ON 18 OCT 2007
L1 470 S LNP
L2 4688 S LMP
L3 6 S L2 AND HIV TAT
L4 6 DUP REM L3 (0 DUPLICATES REMOVED)
L5 2691 S LMP1
L6 4124 S L5 OR LMP 1
L7 6 S L6 AND PROTEIN TRANSDUCTION DOMAIN
L8 4 S BMP AND PROTEIN TRANSDUCTION DOMAIN
L9 4 DUP REM L8 (0 DUPLICATES REMOVED)
L10 6 S BMP AND HIV TAT
L11 6 DUP REM L10 (0 DUPLICATES REMOVED)
L12 25913 S L2 OR L6 OR BMP
L13 1365 S L12 AND (CHIMER? OR FUSION OR HYBRID OR CONJUGA?)
L14 593 S L13 AND (BONE FORM? OR PROTEOGLYCAN OR DIFFERENT?)
L15 354 DUP REM L14 (239 DUPLICATES REMOVED)
L16 167 S L15 AND PY<=2003

=> s l12 and (HIV TAT or VP 22 or Pep 1 or Ant or signal peptide)
L17 70 L12 AND (HIV TAT OR VP 22 OR PEP 1 OR ANT OR SIGNAL PEPTIDE)

=> dup rem l17
PROCESSING COMPLETED FOR L17
L18 51 DUP REM L17 (19 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 51 ANSWERS - CONTINUE? Y/(N):y

L18 ANSWER 1 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1064219 CAPLUS <<LOGINID::20071018>>
TI Detection of gene expression by specific cell types in mixed samples or tissues such as mouse thymus cortex or medullary stromal cells using DGEM (differential gene expression mapping)
IN Petrie, Howard T.
PA USA
SO PCT Int. Appl., 257pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007106507	A2	20070920	WO 2007-US6363	20070314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-782124P P 20060314
AB Differential gene expression mapping (DGEM) utilizes (1) laser capture microdissection or other methods of microdissection of the tissue regions of interest; (2) microarray screening of RNA isolated from the microdissected regions and anal. of purified individual cellular components from the tissue; (3) and computational profiling or subtraction to identify gene expression by specific cell types in situ. The method was applied to stromal cells from whole cortical and medullary regions of C57BL6 mouse thymus. As a result, DGEM, a reverse identification approach, solves previously insurmountable problems, as the lymphoid progenitors can be readily isolated, allowing fluctuations in receptor expression on lymphoid cells to be used to predict stratified stromal signals. An algorithmic approach can be used for calcg. the expression profile of a tissue/sample of interest that consists of at least two types of cells. Specifically, the approach electronically subtracts the expression profile of one component of a sample from the expression profile of the total sample, thus revealing the profiles of the other component. To confirm the robustness of the DGEM procedure, the gene expression profiles from each sample of whole medulla, whole cortex, cortical thymocytes and medullary thymocytes was sorted based only on the expression data.

L18 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563369 CAPLUS <<LOGINID::20071018>>
DN 147:1976
TI Mechanisms of osteoinduction by ***LMP*** - ***1*** (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by ***LMP*** and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA Warsaw Orthopedic, Inc., USA; Emory University
SO PCT Int. Appl., 126pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058878	A2	20070524	WO 2006-US43610	20061109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI US 2005-736191P P 20051110
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptidomimetics of LIM domain-contg. mineralization proteins (LMPs), particularly ***LMP*** - ***1*** (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. The inventors discovered that ***LMP*** - ***1*** can increase cellular responsiveness of mesenchymal stem cells to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of ***LMP*** - ***1*** . It is further demonstrated that ***LMP*** - ***1*** interacts in vitro an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. ***LMP*** - ***1*** interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in ***LMP*** - ***1*** , and can be mimicked by a small peptide contg. only that motif. Further, ***LMP*** - ***1*** competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also ***LMP*** - ***1*** is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L18 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538755 CAPLUS <<LOGINID::20071018>>
DN 147:3135
TI Bone morphogenetic protein 7 plasmid-based gene therapy for renal failure
IN Fisher, Laurent Bernard
PA Merial Ltd., USA
SO PCT Int. Appl., 59pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056614	A1	20070518	WO 2006-US44048	20061114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007155688	A1	20070705	US 2006-599026	20061114

PRAI US 2005-736452P P 20051114
AB The present invention relates to recombinant vectors expressing the ***BMP*** -7 polypeptide in host cells and to pharmaceutical compns. comprising such recombinant vectors. The invention also encompasses methods for prevention and/or treatment of both acute and chronic renal failure in mammals, advantageously in dogs and cats, by administration of the recombinant vectors and pharmaceutical compns. of the invention.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:117791 CAPLUS <<LOGINID::20071018>>
DN 146:203915
TI Gene expression profile for diagnosing small cell lung cancer, discriminating from non-small cell lung cancer, and assessing chemotherapy-resistant lung cancer
IN Nakamura, Yusuke; Daigo, Yataro; Nakatsuru, Shuichi
PA Oncotherapy Science, Inc., Japan; The University of Tokyo
SO PCT Int. Appl., 215pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007013665	A2	20070201	WO 2006-JP315254	20060726
WO 2007013665	A3	20070705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRAI US 2005-703192P P 20050727
US 2006-799961P P 20060511
AB Methods for detecting and diagnosing small cell lung cancer (SCLC) are described. In one embodiment, the diagnostic method involves detg. the expression level of an SCLC-assocd. gene that discriminates between SCLC cells and normal cells. In another embodiment, the diagnostic method involves detg. the expression level of an SCLC-assocd. gene that distinguishes two major histol. types of lung cancer, i.e., non-small cell lung cancer (NSCLC) and SCLC. Finally, the present invention provides methods of screening for therapeutic agents useful in the treatment of small cell lung cancer, methods of treating small cell lung cancer, and methods for vaccinating a subject against small cell lung cancer. Furthermore, the present invention provides chemotherapy-resistant lung cancer- or SCLC-assocd. genes as diagnostic markers and/or mol. targets for therapeutic agent for these cancers. These genes are up-regulated in chemoresistant lung cancer or SCLC. Accordingly, chemoresistant lung cancer or SCLC can be predicted using expression level of the genes as diagnostic markers. As the result, any adverse effects caused by ineffective chemotherapy can be avoided, and more suitable and effective therapeutic strategy can be selected.

L18 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912734 CAPLUS <<LOGINID::20071018>>
DN 147:269173
TI CAMK2 phosphorylation-related mechanism of osteoinduction by ***LMP*** -3 (LIM domain-containing mineralization protein 3), and osteogenic compositions therefor
IN Boden, Scott D.; Sangadala, Sreedhara
PA USA
SO U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 385,612.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007191591	A1	20070816	US 2006-633963	20061205
US 2007027081	A1	20070201	US 2006-385612	20060321

PRAI US 2006-772322P P 20060210
US 2006-385612 A2 20060321
US 2005-664073P P 20050322
US 2005-664074P P 20050322
US 2005-736191P P 20051110
AB The invention provides novel osteogenic compns. based on Smad ubiquitin regulatory factor-1 (Smurf1)-independent methods of osteoinduction using ***LMP*** -3 (LIM domain-contg. mineralization protein 3). The inventors

discovered that a unique amino acid sequence (QNGCRPLTNSRSDRWSQMP) in ***LMP*** -3 C-terminus contains a calmodulin kinase 2 (CAMK2) phosphorylation site (QNGCRPLTNSRSDRW). It was also discovered, that ***LMP*** -3 competes with Smad1 for phosphorylation by CAMK2. In a broad aspect, the compn. comprises either a first amino acid sequence which is capable of being phosphorylated by CAMK2; or a nucleic acid sequence encoding the first amino acid sequence; or a combination thereof. Optionally, the first amino acid sequence may further comprise a second amino acid sequence which is capable of binding the Smurf1 protein. Further, the compn. may comprise a ***BMP*** (bone morphogenetic protein) and/or an agent capable of decreasing an amt. or an activity of CAMK2. The compns. of the instant invention may be incorporated into an implant or delivered via a catheter.

L18 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:229584 CAPLUS <<LOGINID::20071018>>
DN 147:273365
TI A novel TAT fusion protein with osteoinductive activity
AU Zhang, Da-Wei; Li, Li-Wen; Hu, Yun-Yu
CS Institute of Orthopaedics, Xijing Hospital, The Fourth Military Medical University, Xian, 710032, Peop. Rep. China
SO Medical Hypotheses (2007), 68(5), 1009-1011
CODEN: MEHYDY; ISSN: 0306-9877
PB Elsevier Ltd.
DT Journal; General Review
LA English
AB A review. Summary: Osteoblasts are thought to be differentiated from pluripotent mesenchymal stem cells. Several intracellular and extracellular osteoinductive proteins are involved in this process. Such proteins include the bone morphogenetic proteins (BMPs) and the LIM mineralization proteins (LMPs) etc. ***LMP*** - ***1*** is a novel LIM domain protein promoting the differentiation of osteoblasts during bone formation. It contains three LIM domains/motifs, one PDZ domain and a unique sequence. Through anal. of the amino acid sequence and the function of the LMPs, it has been found that the PDZ domain (1-93aa) and a unique region (94-133aa) appear to be crit. for bone formation. The TAT protein of human immunodeficiency virus can be fused with other macromols., peptides or proteins and transport them into cells successfully. Once being transduced into cells, the fusion protein can recover its biol. activity through being rapidly refolded. We supposed that TAT could be fused with ***LMP*** - ***1*** (1-133aa) and ***LMP*** - ***1*** (94-133aa) and the fusion proteins could be easily transduced through biol. membranes and generate biol. activity. The clin. application of BMPs has been limited for their relatively high cost and the unstable osteoinductivity. If the hypothesis proved to be practical, we would have a more effective new way to promote bone repair and regeneration.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of osteoinduction by ***LMP*** - ***1*** (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by ***LMP*** and ***BMP*** agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-664073P P 20050322
US 2005-664074P P 20050322
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly ***LMP*** - ***1*** (LIM mineralization protein-1), to overcome the dose-related translational barriers for ***BMP*** -2 (bone morphogenetic protein 2) therapeutics. ***LMP*** and ***BMP*** agents also include peptide or peptidomimetics-encoding oligonucleotides and ***LMP*** and ***BMP*** genes. The inventors discovered that ***LMP*** - ***1*** can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to ***BMP*** -2 and mechanistic elucidation of various aspects of the signaling pathway of ***LMP*** - ***1*** . It is further demonstrated that ***LMP*** - ***1*** interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of ***BMP*** -2 signaling mols., Smad1 and Smad5. ***LMP*** - ***1*** interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in ***LMP*** - ***1*** , and can be mimicked by a small peptide contg. only that motif. Further, ***LMP*** - ***1*** competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to ***BMP*** -2. Also ***LMP*** - ***1*** is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L18 ANSWER 8 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2006563307 EMBASE <<LOGINID::20071018>>
TI Schnurri transcription factors from Drosophila and vertebrates can mediate ***Bmp*** signaling through a phylogenetically conserved mechanism.
AU Yao L.-C.; Bitz I.L.; Peiffer D.A.; Phin S.; Wang Y.; Ogata S.; Cho K.W.Y.; Arora K.; Warrior R.
CS K. Arora, Department of Developmental and Cell Biology, Developmental Biology Center, University of California Irvine, Irvine, CA 92697, United States. karora@uci.edu
SO Development, (Oct 2006) Vol. 133, No. 20, pp. 4025-4034.
Refs: 56
ISSN: 0950-1991 CODEN: DEVPED
CY United Kingdom
DT Journal; Article
FS 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 7 Dec 2006
Last Updated on STN: 7 Dec 2006
AB Bone Morphogenetic Proteins (Bmps) are secreted growth factors that play crucial roles in animal development across the phylogenetic spectrum. ***Bmp*** signaling results in the phosphorylation and nuclear translocation of Smads, downstream signal transducers that bind DNA. In Drosophila, the zinc finger protein Schnurri (Shn) plays a key role in signaling by the Bmp2/Bmp4 homolog Decapentaplegic (Dpp), by forming a Shn/Smad repression complex on defined promoter elements in the brinker (brk) gene. Brk is a transcriptional repressor that downregulates Dpp target genes. Thus, brk inhibition by Shn results in the upregulation of Dpp-responsive genes. We present evidence that vertebrate Shn homologs can also mediate ***Bmp*** responsiveness through a mechanism similar to Drosophila Shn. We find that a ***Bmp*** response element (BRE) from the Xenopus Vent2 promoter drives Dpp-dependent expression in Drosophila. However, in sharp contrast to its activating role in vertebrates, the frog BRE mediates repression in Drosophila. Remarkably, despite these opposite transcriptional polarities, sequence changes that abolish cis-element activity in Drosophila also affect BRE function in Xenopus. These similar cis requirements reflect conservation of trans-acting factors, as human Shn1 (hShn1; HIVEP1) can interact with Smad1/Smad4 and assemble an hShn1/Smad complex on the BRE. Furthermore, both Shn and hShn1 activate the BRE in Xenopus embryos, and both repress brk and rescue embryonic patterning defects in shn mutants. Our results suggest that vertebrate Shn proteins function in ***Bmp*** signal transduction, and that Shn proteins recruit co-activators and co-repressors in a context-dependent manner, rather than acting as dedicated activators or repressors.

L18 ANSWER 9 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2007:34447 BIOSIS <<LOGINID::20071018>>
DN PREV200700024339
TI Inflammation and cancer: How hot is the link?.
AU Aggarwal, Bharat B. [Reprint Author]; Shishodia, Shishir; Sandur, Santosh K.; Pandey, Manoj K.; Sethi, Gautam
CS Univ Texas, MD Anderson Canc Ctr, Dept Expt Therapeut, Cytokine Res Lab, 1515 Holcombe Blvd, Houston, TX 77030 USA
aggarwal@mdanderson.org
SO Biochemical Pharmacology, (NOV 30 2006) Vol. 72, No. 11, pp. 1605-1621.
CODEN: BCPCA6. ISSN: 0006-2952.
DT Article
LA English
ED Entered STN: 27 Dec 2006
Last Updated on STN: 27 Dec 2006
AB Although inflammation has long been known as a localized protective reaction of tissue to irritation, injury, or infection, characterized by pain, redness, swelling, and sometimes loss of function, there has been a new realization about its role in a wide variety of diseases, including cancer. While acute inflammation is a part of the defense response, chronic inflammation can lead to cancer, diabetes, cardiovascular, pulmonary, and neurological diseases. Several pro-inflammatory gene products have been identified that mediate a critical role in suppression of apoptosis, proliferation, angiogenesis, invasion, and metastasis. Among these gene products are TNF and members of its superfamily, IL-1 alpha, IL-1 beta, IL-6, IL-8, IL-18, chemokines, MMP-9, VEGF, COX-2, and 5-LOX. The expression of all these genes are mainly regulated by the transcription factor NF-kappa B, which is constitutively active in most

tumors and is induced by carcinogens (such as cigarette smoke), tumor promoters, carcinogenic viral proteins (***HIV*** - ***tat*** , HIV-nef, HIV-vpr, KHSV, EBV- ***LMP1*** , HTLV1-tax, HPV, HCV, and HBV), chemotherapeutic agents, and gamma-irradiation. These observations imply that anti-inflammatory agents that suppress NF-kappa B or NF-kappa B-regulated products should have a potential in both the prevention and treatment of cancer. The current review describes in detail the critical link between inflammation and cancer. (c) 2006 Elsevier Inc. All rights reserved.

L18 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1740600	A1	20070110	EP 2004-749433	20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007505621	T	20070315	JP 2006-526862	20040413
CN 1934123	A	20070321	CN 2004-80008027	20040413
IN 2005KN02097	A	20070810	IN 2005-KN2097	20051024
PRAI US 2003-456551P	P	20030324		
WO 2004-US9127	W	20040413		

AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , ***VP*** - ***22*** , a growth factor ***signal*** ***peptide*** sequence, ***Pep*** - ***1*** , etc.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2
AN 2005:327951 BIOSIS <<LOGINID::20071018>>
DN PREV200510116782
TI Identification of an astacin-like metallo-proteinase transcript from the infective larvae of Strongyloides stercoralis.
AU Gallego, Sara Gomez; Loukas, Alex; Slade, Robert W.; Neva, Franklin A.; Varatharajalu, Ravi; Nutman, Thomas B.; Brindley, Paul J. [Reprint Author]
CS Tulane Univ, Hlth Sci Ctr, Dept Trop Med, Sch Publ Hlth and Trop Med, SL17,1430 Tulane Ave, New Orleans, LA 70112 USA
paul.brindley@tulane.edu
SO Parasitology International, (JUN 2005) Vol. 54, No. 2, pp. 123-133. ISSN: 1383-5769.
DT Article
LA English
ED Entered STN: 25 Aug 2005
Last Updated on STN: 25 Aug 2005
AB Strongyloides stercoralis, an important nematode pathogen of humans, is transmitted by contact with soil contaminated with the microscopic larvae of the parasite. We determined the cDNA sequence and deduced amino acid structure of a metallo-proteinase that is abundantly transcribed expressed by infective stage larvae of S. stercoralis. This deduced structure of the enzyme revealed a multi-domain protein that included an NH2-terminal peptidase. This peptidase consisted of a ***signal*** ***peptide*** , a pro-enzyme region, and a mature peptidase domain that included the metal ion co-ordinating motifs, HETSHALGVIH and SIMHY ("Met-turn"), characteristic of the catalytic active site of members of the metzincin superfamily of zinc metallo-endopeptidases. It was phylogenetically and structurally similar to astacin from the digestive gland of the crayfish Astacus astacus, to the HCH-1 peptidase of Caenorhabditis elegans required for hatching and migration of a post-embryonic neuroblast, and to the morphogenetically important peptidases, bone morphogenetic protein-1 (***BMP*** -1) and Drosophila tolloid. In addition, the Strongyloides enzyme, designated strongylastacin, includes a central epidermal growth factor (EGF) domain followed by a carboxyl CUB (complement sub component C1r/C1s/embryonic sea urchin protein Uegf/bone morphogenetic protein) domain. Inspection of the dbEST database revealed the presence of at least 9 transcript clusters that are related to greater or lesser extent to strongylastacin; based on these expressed sequence tags, strongylastacin was expressed only in the infective third stage larvae, whereas other transcript clusters were expressed both in filariform and rhabditiform stages or only in the rhabditiform stage. Based on the deduced sequence, structure, and expression profile, strongylastacin is the probable candidate for the zinc-dependent metalloprotease, Ss40, known to be deployed by larvae of S. stercoralis to penetrate human skin to initiate infection. (c) 2005 Elsevier Ireland Ltd. All rights reserved.

L18 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:971289 CAPLUS <<LOGINID::20071018>>
DN 143:265304
TI Proliferative activity of extracellular HIV-1 Tat protein in human epithelial cells: Expression profile of pathogenetically relevant genes
AU Bettaccini, Alessia A.; Baj, Andreina; Accolla, Roberto S.; Basolo, Fulvio; Toniolo, Antonio Q.
CS Dipartimento di Scienze Cliniche e Biologiche, Universita dell' Insubria, Varese, Italy
SO BMC Microbiology (2005), 5, No pp. given
CODEN: BMMIBC; ISSN: 1471-2180
URL: http://www.biomedcentral.com/content/pdf/1471-2180-5-20.pdf
PB BioMed Central Ltd.
DT Journal; (online computer file)
LA English
AB Tat is being tested as a component of HIV vaccines. Tat activity has been mainly investigated on cells of lymphoid/hematopoietic lineages. HIV-1, however, is known to infect many different cells of both solid organs and mucosal surfaces. The activity of 2-exon (aa 1-101) and synthetic (aa 1-86) Tat was studied on mammary and amniotic epithelial cells cultured under low serum conditions. Small concns. of Tat (100 ng/mL) stimulated cell proliferation. Tat antibodies neutralized the mitogenic Tat activity. Changes of gene expression in Tat-treated cells were evaluated by RT-PCR and gene-array methods. Within 4 h of treatment, exposure to Tat is followed by up-regulation of some cell cycle-assocd. genes (transcription factors, cyclin/cdk complexes, genes of apoptotic pathways) and of genes relevant to HIV pathogenesis [chemokine receptors (CXCR4, CCR3), chemotactic cytokines (SDF-I, RANTES, SCYCI, SCYEI), IL6 family cytokines, inflammatory cytokines, factors of the TGF-.beta. family (TGFb, ***BMP*** -1, ***BMP*** -2)]. Upregulation of anti-inflammatory cytokines (IL-10, IL-19, IL-20), a hallmark of other persistent viral infections, was a remarkable feature of Tat-treated epithelial cell lines. Thus, extracellular Tat is mitogenic for mammary and amniotic epithelial cells and stimulates the expression of genes of pathogenic interest in HIV infection. These effects may favor virus replication and may facilitate the mother-to-child transmission of virus.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:825023 CAPLUS <<LOGINID::20071018>>
DN 141:325787
TI Intracellular delivery expression construct encoding fusion protein of osteoinductive proteins and peptides and use to induce bone formation
IN Titus, Frances Louisa; Marx, Jeffrey C.; Boden, Scott D.; Yoon, Sangwook T.; Drapeau, Susan
PA USA
SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004197867	A1	20041007	US 2004-806915	20040323
CA 2517496	A1	20040924	CA 2004-2517496	20040324
AU 2004317501	A1	20051124	AU 2004-317501	20040324
PRAI US 2003-456551P	P	20030324		

AB The present invention provides a method of producing a cell-permeable osteoinductive polypeptide comprising introducing into a suitable host cell an expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide positioned so that the osteoinductive polypeptide is expressed as part of a fusion protein with the cell-permeable polypeptide. The invention also provides osteoinductive peptides which have demonstrated the ability to induce bone formation in vivo. The invention further relates to that the cell-permeable polypeptide may be chosen from the group consisting of ***HIV*** - ***TAT*** , ***VP*** - ***22*** , a growth factor ***signal*** ***peptide*** sequence, ***Pep*** - ***1*** , etc.

L18 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:60034 CAPLUS <<LOGINID::20071018>>
DN 140:130147
TI Methods for stimulating differentiation of stem cells into cardiac cells by using Wnt antagonists or Dkk proteins
IN Lassar, Andrew B.; Mercola, Mark; Gupta, Ruchika; Marvin, Martha; Schneider, Valerie; Tzahor, Eldad; Brott, Barbara; Sokol, Sergei
PA USA

SO U.S. Pat. Appl. Publ., 62 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004014209	A1	20040122	US 2003-351275	20030123

PRAI US 2002-351126P P 20020123
US 2002-352456P P 20020128
US 2002-352665P P 20020129
AB The present invention relates to compns. and methods for stimulating differentiation of stem cells into cardiac cells by using Wnt antagonists or Dkk proteins. The methods of the invention involve contacting a population cells comprising stem cells with at least one Wnt antagonist, such as a polypeptide or polypeptide fragment. In certain embodiments, the methods of the invention involve Dkk proteins or fragments, homologs, derivs., variants, or peptidomimetics thereof.

L18 ANSWER 15 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 3
AN 2004:352745 BIOSIS <<LOGINID::20071018>>
DN PREV200400353283
TI Large-scale analysis of the genes involved in fin regeneration and blastema formation in the medaka, Oryzias latipes.
AU Katogi, Rei; Nakatani, Yuki; Shin-i, Tadasu; Kohara, Yuji; Inohaya, Keiji; Kudo, Akira [Reprint Author]
CS Dept Biol InformatMidori Ku, Tokyo Inst Technol, 4259 Nagatsuta, Yokohama, Kanagawa, 2268501, Japan
akudo@bio.titech.ac.jp
SO Mechanisms of Development, (July 2004) Vol. 121, No. 7-8, pp. 861-872. print.
CODEN: MEDVE6. ISSN: 0925-4773.
DT Article
LA English
ED Entered STN: 26 Aug 2004
Last Updated on STN: 26 Aug 2004
AB Medaka is an attractive model to study epimorphic regeneration. The fins have remarkable regenerative capacity and are replaced about 14 days after amputation. The formation of blastema, a mass of undifferentiated cells, is essential for regeneration; however, the molecular mechanisms are incompletely defined. To identify the genes required for fin regeneration, especially for blastema formation, we constructed cDNA libraries from fin regenerates at 3 days postamputation and 10 days postamputation. A total of 16,866 expression sequence tags (ESTs) were sequenced and subjected to BLASTX analysis. The result revealed that about 60% of them showed strong matches to previously identified proteins, and major signaling molecules related to development, including FGF, ***BMP*** , Wnt, Notch/Delta, and Ephrin/Eph signaling pathways were isolated. To identify novel genes that showed specific expression during fin regeneration, cDNA microarray was generated based on 2900 independent ESTs from each library which had no sequence similarity to known proteins. We obtained 6 candidate genes associated with blastema formation by gene expression pattern screening in competitive hybridization analyses and in situ hybridization. Olrfe16d23 and olrfe14k04 were expressed only in early regenerating stages when blastema formation was induced. The expression of olrf5n23, which encodes a novel ***signal*** ***peptide*** , was detected in wound epidermis throughout regeneration. Olrfe23122, olrfe20n22 and olrfe24i02 were expressed notably in the blastema region. Our study has thus identified the gene expression profiles and some novel candidate genes to facilitate elucidation of the molecular mechanisms of fin regeneration. Copyright 2004 Elsevier Ireland Ltd. All rights reserved.

L18 ANSWER 16 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 4
AN 2004:358689 BIOSIS <<LOGINID::20071018>>
DN PREV200400363883
TI Identification and characterization of human CKTSF1B2 and CKTSF1B3 genes in silico.
AU Katoh, Masuko [Reprint Author]; Katoh, Masaru
CS Inst ResGenet and Cell Biol SectChuo Ku, Natl Canc Ctr, Tsukiji 5-Chome, Tokyo, 1040045, Japan
mkatoh@ncc.go.jp
SO Oncology Reports, (August 2004) Vol. 12, No. 2, pp. 423-427. print.
ISSN: 1021-335X.
DT Article
LA English
ED Entered STN: 5 Sep 2004
Last Updated on STN: 5 Sep 2004
AB Bone morphogenetic proteins (BMPs) are implicated in the regulation of morphogenesis and proliferation during embryogenesis and carcinogenesis. We have previously reported over-expression of BMP4 in diffuse-type gastric cancer cells. ***BMP*** signaling is regulated by tissue-specific expression of ligands and receptors as well as by secreted-type antagonists, such as CKTSF1B1 (Gremlin), CER1 (Cerberus 1), Noggin, SOSTDC1 (Ectodin), and Chordin. Here, we identified two novel genes related to CKTSF1B1 and CER1 by using bioinformatics. Two novel members of human CKTSF1B gene family were designated CKTSF1B2 (GREM2 or PRDC) and CKTSF1B3 (GREM3 or DANTE). FLJ21195 (BC046632.1) was the representative human CKTSF1B2 cDNA, and CKTSF1B2 gene was mapped to human chromosome 1q43. Human CKTSF1B2 showed 94.0% total amino-acid identity with mouse Cktsf1b2 (Prdc). FLJ38607 (AK095926.1) was the representative human CKTSF1B3 cDNA, and CKTSF1B3 gene was mapped to human chromosome 19p13.2. Human CKTSF1B3 showed 61.9% total amino-acid identity with mouse Cktsf1b2 (Dante). N-terminal ***signal*** ***peptide*** and DAN domain with nine cysteine residues were conserved among CKTSF1B1, CKTSF1B2, CKTSF1B3 and CER1. Phylogenetic analyses revealed that CKTSF1B2 was more related to CKTSF1B1, and that CKTSF1B3 was more related to CERL CKTSF1B1, CKTSF1B2, CKTSF1B3 and CER1 constitute the CKTSF1B family among secreted-type cysteine knot superfamily proteins. This is the first report on identification and characterization of the human CKTSF1B2 and CKTSF1B3 genes.

L18 ANSWER 17 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004026296 EMBASE <<LOGINID::20071018>>
TI Expression of bone morphogenetic protein-6 and -2 and a bone morphogenetic protein antagonist in horses with naturally acquired osteochondrosis.
AU Semevolos S.A.; Nixon A.J.; Strassheim M.L.
CS Dr. S.A. Semevolos, Comparative Orthopaedics Laboratory, Department of Clinical Sciences, Cornell University, Ithaca, NY 14853, United States
SO American Journal of Veterinary Research, (Jan 2004) Vol. 65, No. 1, pp. 110-115.
Refs: 18
ISSN: 0002-9645 CODEN: AJVRAH
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
033 Orthopedic Surgery
005 General Pathology and Pathological Anatomy
LA English
SL English
ED Entered STN: 29 Jan 2004
Last Updated on STN: 29 Jan 2004
AB Objective - To determine the mRNA expression of bone morphogenetic protein (***BMP***)-6 and -2 and a ***BMP*** antagonist (Noggin) in horses with osteochondrosis. Sample Population - Samples of articular cartilage from affected stifle or shoulder joints of 10 immature horses with naturally acquired osteochondrosis and corresponding joints of 9 clinically normal horses of similar age; additionally, samples of distal femoral growth plate cartilage and distal femoral articular cartilage were obtained from a normal equine fetus. Procedure - Cartilage specimens were snap-frozen in liquid nitrogen, and total RNA was isolated. Adjacent specimens were fixed in 4% paraformaldehyde for histologic examination. Expression of ***BMP*** -6, ***BMP*** -2, and Noggin mRNA was evaluated by real-time quantitative polymerase chain reaction (PCR) assays. Spatial tissue mRNA expression of ***BMP*** -6 was determined by in situ hybridization. Results - Nucleotide sequences were obtained for portions of the ***BMP*** -6 propeptide and mature peptide region, as well as the signal and mature peptide region of Noggin. Expression of ***BMP*** -6, ***BMP*** -2, and Noggin mRNA was found to be similar in cartilage from normal and osteochondrosis-affected horses. Spatial expression of ***BMP*** -6 correlated with the middle and deep layers of articular cartilage; no differences were observed in overall expression between cartilage specimens from the 2 groups of horses. No expression of ***BMP*** -6 was found in the superficial layer, subchondral bone, or osteochondrosis-affected cleft fibrous tissue. Conclusions and Clinical Relevance - Although these signaling peptides may play important roles in cartilage differentiation, results did not provide evidence to suggest that they are involved in the disease process of osteochondrosis.

L18 ANSWER 18 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
AN 2004:302643 BIOSIS <<LOGINID::20071018>>
DN PREV200400303074
TI hCHL2, a novel chordin-related gene, displays differential expression and complex alternative splicing in human tissues and during myoblast and osteoblast maturation.
AU Oren, Anat; Toporik, Amir; Biton, Sharon; Almogy, Nechama; Eshel, Dani; Bernstein, Jeanne; Savitsky, Kinneret; Rotman, Galit [Reprint Author]
CS Compugen Ltd, 72 Pinchas Rosen St, IL-69512, Tel Aviv, Israel
galltr@compugen.co.il
SO Gene (Amsterdam), (April 28 2004) Vol. 331, No. April 28, pp. 17-31. print.
ISSN: 0378-1119 (ISSN print).
DT Article
LA English
ED Entered STN: 30 Jun 2004
Last Updated on STN: 30 Jun 2004
AB Chordin-like cysteine-rich repeats (CRs) are conserved domains present in an expanding family of secreted proteins that associate with members of the TGFbeta superfamily. In this study, we report the molecular cloning and characterization of CHL2 (chordin-like 2), a novel protein closely related to CHL (chordin-like). Both are members of the chordin family of proteins, and contain a ***signal*** ***peptide*** and three CR

domains. We found that recombinant human CHL2 (hCHL2) protein is secreted and binds activin A, but not ***BMP*** -2, -4, or -6. Expression of hCHL2 mRNA and protein was detected in a variety of human tissues and is particularly abundant in the uterus. Extensive and complex alternative splicing of hCHL2 was observed in different tissues, resulting in several distinct protein isoforms that vary substantially in the presence of a ***signal*** ***peptide*** and their content of CR domains. Differential expression of CHL2 variants was observed during myoblast and osteoblast differentiation, implying a role for this gene in these physiological processes. Copyright 2004 Elsevier B.V. All rights reserved.

L18 ANSWER 19 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004175040 EMBASE <<LOGINID::20071018>>
TI hCHL2, a novel chordin-related gene, displays differential expression and complex alternative splicing in human tissues and during myoblast and osteoblast maturation.
AU Oren A.; Toporik A.; Biton S.; Almogy N.; Eshel D.; Bernstein J.; Savitsky K.; Rotman G.
CS G. Rotman, Compugen Ltd., 72 Pinchas Rosen St., Tel Aviv 69512, Israel. galitr@compugen.co.il
SO Gene, (28 Apr 2004) Vol. 331, No. 1-2, pp. 17-31.
Refs: 37
ISSN: 0378-1119 CODEN: GENED6
PUI S 0378-1119(04)00018-6
CY Netherlands
DT Journal; Article
FS 022 Human Genetics
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 13 May 2004
Last Updated on STN: 13 May 2004
AB Chordin-like cysteine-rich repeats (CRs) are conserved domains present in an expanding family of secreted proteins that associate with members of the TGF.beta. superfamily. In this study, we report the molecular cloning and characterization of CHL2 (chordin-like 2), a novel protein closely related to CHL (chordin-like). Both are members of the chordin family of proteins, and contain a ***signal*** ***peptide*** and three CR domains. We found that recombinant human CHL2 (hCHL2) protein is secreted and binds activin A, but not ***BMP*** -2, -4, or -6. Expression of hCHL2 mRNA and protein was detected in a variety of human tissues and is particularly abundant in the uterus. Extensive and complex alternative splicing of hCHL2 was observed in different tissues, resulting in several distinct protein isoforms that vary substantially in the presence of a ***signal*** ***peptide*** and their content of CR domains. Differential expression of CHL2 variants was observed during myoblast and osteoblast differentiation, implying a role for this gene in these physiological processes. .COPYRGT. 2004 Elsevier B.V. All rights reserved.

L18 ANSWER 20 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
AN 2003:390222 BIOSIS <<LOGINID::20071018>>
DN PREV200300390222
TI BMPER, a novel endothelial cell precursor-derived protein, antagonizes bone morphogenetic protein signaling and endothelial cell differentiation.
AU Moser, Martin; Binder, Olav; Wu, Yaxu; Aitsebaomo, Julius; Ren, Rongqin; Bode, Christoph; Bautch, Victoria L.; Conlon, Frank L.; Patterson, Cam [Reprint Author]
CS Carolina Cardiovascular Biology Center, University of North Carolina at Chapel Hill, 5.109C Neurosciences Building, Chapel Hill, NC, 27599-7126, USA
cpatters@med.unc.edu
SO Molecular and Cellular Biology, (August 2003) Vol. 23, No. 16, pp. 5664-5679. print.
ISSN: 0270-7306 (ISSN print).
DT Article
LA English
ED Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003
AB The development of endothelial cell precursors is essential for vasculogenesis. We screened for differentially expressed transcripts in endothelial cell precursors in developing mouse embryoid bodies. We cloned a complete cDNA encoding a protein that contains an amino-terminal ***signal*** ***peptide*** , five cysteine-rich domains, a von Willebrand D domain, and a trypsin inhibitor domain. We termed this protein BMPER (bone morphogenetic protein (***BMP***)-binding endothelial cell precursor-derived regulator). BMPER is specifically expressed in flk-1-positive cells and parallels the time course of flk-1 induction in these cells. In situ hybridization in mouse embryos demonstrates dorsal midline staining and staining of the aorto-gonadal-mesonephric region, which is known to host vascular precursor cells. BMPER is a secreted protein that directly interacts with BMP2, BMP4, and BMP6 and antagonizes BMP4-dependent Smad5 activation. In Xenopus embryos, ventral injection of BMPER mRNA results in axis duplication and downregulation of the expression of Xvent-1 (downstream target of Smad signaling). In an embryoid body differentiation assay, BMP4-dependent differentiation of endothelial cells in embryoid bodies is also antagonized by BMPER. Taken together, our data indicate that BMPER is a novel ***BMP*** -binding protein that is expressed by endothelial cell precursors, has ***BMP*** -antagonizing activity, and may play a role in endothelial cell differentiation by modulating local ***BMP*** activity.

L18 ANSWER 21 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2003309677 EMBASE <<LOGINID::20071018>>
TI Suppression of macho-1-directed muscle fate by FGF and ***BMP*** is required for formation of posterior endoderm in ascidian embryos.
AU Kondoh K.; Kobayashi K.; Nishida H.
CS H. Nishida, Department of Biological Sciences, Tokyo Institute of Technology, Nagatsuta, Yokohama 226-8501, Japan. hnishida@bio.titech.ac.jp
SO Development, (Jul 2003) Vol. 130, No. 14, pp. 3205-3216.
Refs: 54
ISSN: 0950-1991 CODEN: DEVPED
CY United Kingdom
DT Journal; Article
FS 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 14 Aug 2003
Last Updated on STN: 14 Aug 2003
AB Specification of germ layers is a crucial event in early embryogenesis. In embryos of the ascidian, Halocynthia roretzi, endoderm cells originate from two distinct lineages in the vegetal hemisphere. Cell dissociation experiments suggest that cell interactions are required for posterior endoderm formation, which has hitherto been thought to be solely regulated by localized egg cytoplasmic factors. Without cell interaction, every descendant of posterior-vegetal blastomeres, including endoderm precursors, assumed muscle fate. Cell interactions are required for suppression of muscle fate and thereby promote endoderm. differentiation in the posterior endoderm precursors. The cell interactions take place at the 16- to 32-cell stage. Inhibition of cell signaling by FGF receptor and MEK inhibitor also supported the requirement of cell interactions. Consistently, FGF was a potent signaling molecule, whose signaling is transduced by MEK-MAPK. By contrast, such cell interactions are not required for formation of the anterior endoderm. Our results suggest that another redundant signaling molecule is also involved in the posterior endoderm formation, which is likely to be mediated by ***BMP*** . Suppression of the function of macho-1, a muscle determinant in ascidian eggs, by antisense oligonucleotide was enough to allow autonomous endoderm specification. Therefore, the cell interactions induce endoderm formation by suppressing the function of macho-1, which is to promote muscle fate. These findings suggest the presence of novel mechanisms that suppress functions of inappropriately distributed maternal determinants via cell interactions after embryogenesis starts. Such cell interactions would restrict the regions where maternal determinants work, and play a key role in marking precise boundaries between precursor cells of different tissue types.

L18 ANSWER 22 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004126369 EMBASE <<LOGINID::20071018>>
TI Bone graft substitutes for spinal fusion.
AU Whang P.G.; Wang J.C.
CS Dr. J.C. Wang, Department of Orthopaedic Surgery, University of California, Los Angeles School of Medicine, 10833 LeConte Avenue, Los Angeles, CA 90095-6902, United States
SO Spine Journal, (Mar 2003) Vol. 3, No. 2, pp. 155-165.
Refs: 113
ISSN: 1529-9430 CODEN: SJPOA6
PUI S 1529-9430(02)00539-9
CY United States
DT Journal; General Review; (Review)
FS 022 Human Genetics
030 Clinical and Experimental Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
039 Pharmacy
LA English
ED Entered STN: 1 Apr 2004
Last Updated on STN: 1 Apr 2004

L18 ANSWER 23 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2003330684 EMBASE <<LOGINID::20071018>>
TI Regulation of ovarian function by the TGF-.beta. superfamily and follistatin.
AU Lin S.-Y.; Morrison J.R.; Phillips D.J.; de Kretser D.M.
CS D.M. de Kretser, Centre for Molec. Repro./Endocrinol., Monash Inst. of Reproduction/Devmt., Monash University, Melbourne, Vic. 3168, Australia. david.de.kretser@med.monash.edu.au
SO Reproduction, (1 Aug 2003) Vol. 126, No. 2, pp. 133-148.
Refs: 116
ISSN: 1470-1626 CODEN: RCUKBS
CY United Kingdom
DT Journal; General Review; (Review)
FS 010 Obstetrics and Gynecology
021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
003 Endocrinology

LA English
SL English
ED Entered STN: 4 Sep 2003
Last Updated on STN: 4 Sep 2003
AB The role of follistatin as an activin-binding protein has dominated the study of this molecule for the last 10 years. However, there is emerging evidence that follistatin has a role in modulating the biology of other members of the transforming growth factor .beta. (TGF-.beta.) superfamily. This review summarizes the current concepts encompassing follistatin biochemistry as well as molecules with which it is functionally associated. Moreover, the importance of the two follistatin isoforms (follistatin-288 and follistatin-315) is discussed with particular emphasis on the regulation of the ovary. In addition to activin, this review discusses the functions of other members of the TGF-.beta. superfamily, for example growth differentiation factor 9 (GDF-9), bone morphogenetic protein 15 (***BMP*** -15), ***BMP*** -6, ***BMP*** -4 and ***BMP*** -7, in the ovary, and the potential interactions between follistatin and these growth factors. The complex network of TGF-.beta. superfamily growth factor members involved in the modulation of ovarian function and the interactions of follistatin with these proteins is highlighted.

L18 ANSWER 24 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2006546239 EMBASE <<LOGINID::20071018>>
TI Construction of a eukaryote expression vector containing bone morphogenetic protein-2 mature peptide by SOE-PCR method.
AU Duan X.-H.; Chen S.-M.; Chai Y.-B.; Xu K.-W.
CS X.-H. Duan, School of Material Engineering, Xi'an Jiaotong University, Xi'an 710049, China
SO Chinese Journal of Clinical Rehabilitation, (Dec 2002) Vol. 6, No. 24, pp. 3762-3763.
Refs: 5
ISSN: 1671-5926 CODEN: ZLKHAH
CY China
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 20 Nov 2006
Last Updated on STN: 20 Nov 2006
AB Objective: To construct an eukaryote expression vector containing bone morphogenetic protein-2 (***BMP*** 2) mature peptide. Methods: Gene splicing by overlapping extension PCR (SOE-PCR) method was used to clone BMP2 ***signal*** ***peptide*** and mature peptide and their fusion fragment. The fusion fragment was cloned into an eukaryote expressing vector pcDNA3. 1 / myc-His(-) A. The sequence of the fusion fragment of BMP2 ***signal*** ***peptide*** and mature peptide was identified. Results: The sequence of the fusion fragment was correct comparing with BMP2 ***signal*** ***peptide*** and mature peptide published by NCBI. Conclusion: The vector pcDNA3. 1 / myc-His(-) A-BMP2sm constructed in this experiment was suitable to applying in eukaryotic expression of BMP2.

L18 ANSWER 25 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2002286396 EMBASE <<LOGINID::20071018>>
TI Effects of heterodimerization and proteolytic processing on Derriere and Nodal activity: Implications for mesoderm induction in Xenopus.
AU Eimon P.M.; Harland R.M.
CS R.M. Harland, Department of Molecular/Cell Biology, University of California, Berkeley, CA 94720-3202, United States.
harland@socrates.berkeley.edu
SO Development, (2002) Vol. 129, No. 13, pp. 3089-3103.
Refs: 87
ISSN: 0950-1991 CODEN: DEVPED
CY United Kingdom
DT Journal; General Review; (Review)
FS 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 29 Aug 2002
Last Updated on STN: 29 Aug 2002
AB Derricere is a recently discovered member of the TGF.beta. superfamily that can induce mesoderm in explant assays and is expressed at the right time and location to mediate mesoderm induction in response to VegT during Xenopus embryogenesis. We show that the ability of Derriere to induce dorsal or ventral mesoderm depends strictly on the location of expression and that a dominant-negative Derriere cleavage mutant completely blocks all mesoderm formation when ectopically expressed. This differs from the activity of similar Xnr2 cleavage mutant constructs, which are secreted and retain signaling activity. Additional analysis of mesoderm induction by Derriere and members of the Nodal family indicates that these molecules are involved in a mutual positive-feedback loop and antagonism of either one of the signals can reduce the other. Interaction between Derriere and members of the Nodal family is also shown to occur through the formation of heterodimeric ligands. Using an oocyte expression system we show direct interaction between the mature Derriere ligand and members of both the Nodal and ***BMP*** families. Taken together, these findings indicate that Derriere and Nodal proteins probably work cooperatively to induce mesoderm throughout the marginal zone during early Xenopus development.

L18 ANSWER 26 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2002166590 EMBASE <<LOGINID::20071018>>
TI Lysine residues of Epstein-Barr virus-encoded nuclear antigen 2 do not confer secondary modifications via ubiquitin or SUMO-like proteins but modulate transcriptional activation.
AU Hille A.; Badu-Antwi A.; Holzer D.; Grasser F.A.
CS F.A. Grasser, Institut fur Mikrobiologie/Hygiene, Abteilung Virologie, Universitatskliniken, Haus 47, 66421 Homburg Saar, Germany.
graesser@uniklinik-saarland.de
SO Journal of General Virology, (2002) Vol. 83, No. 5, pp. 1037-1042.
Refs: 27
ISSN: 0022-1317 CODEN: JGVIAY
CY United Kingdom
DT Journal; Article
FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 23 May 2002
Last Updated on STN: 23 May 2002
AB Epstein-Barr virus nuclear antigen 2 (EBNA2) is essential for transformation through activation of viral and cellular genes. Within 487 residues, EBNA2 contains six lysine (K) residues (positions, 335, 357, 359, 363, 366 and 480), which were mutated to arginine (R) residues, either individually or in combination, and tested for subcellular localization, mobility by SDS-PAGE and transactivation of three promoters. All mutants featuring the K(480)R mutation within the nuclear localization signal were partially cytoplasmic with a reduced level of transactivation of the latent membrane protein 1 (***LMP1***) promoter (-327 to +40). The K(366)R mutation also showed a decrease in transactivation of a promoter consisting only of 12 recombination signal-binding protein-J.kappa.-binding sites, while all mutants with the K(335)R exchange showed a markedly elevated transactivation with the -327 to +40 construct and all mutants showed slightly reduced transactivation with a -634 to +40 ***LMP1*** promoter. None of the mutants exhibited altered migration in SDS-PAGE, excluding secondary modification, i.e. through SUMO-like proteins.

L18 ANSWER 27 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:354029 BIOSIS <<LOGINID::20071018>>
DN PREV200200354029
TI Characterization of a potential new fibrillar collagen, type XXIV.
AU Gordon, Marion K. [Reprint author]; Hahn, Rita A. [Reprint author]; Zhou, Peihong [Reprint author]; Bhatt, Pinaki [Reprint author]; Song, Richard [Reprint author]; Kistler, Andrew [Reprint author]; Gerecke, Donald R. [Reprint author]; Koch, Manuel
CS Pharmacology and Toxicology, Rutgers University, 170 Frelinghuysen Rd, Piscataway, NJ, 08854, USA
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A359. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002
AB We have cloned a new collagen cDNA, type XXIV, which appears to be a member of the type V and XI fibrillar collagen subfamily. The C-propeptide domain has 8 conserved cysteines, but the cleavage site for processing is not apparent. At 931 amino acid residues, the triple helical domain is about 90% the length of other fibrillar collagens. The N-peptide is 547 amino acids, similar to type V and XI collagen N-peptides. It contains a ***signal*** ***peptide*** , a 250 residue N-terminal thrombospondin-like domain (Tsp), a region with charged residues and tyrosines, and a minor triple helix. There is no consensus ***BMP*** -1 site within the N-propeptide indicative of processing. On Western blots, an antibody generated against the polypeptide reacts with a apprx145 kDa band. This size is consistent with the removal of the C-propeptide, leaving an unprocessed N-peptide linked to the triple helical domain. RT-PCR of various tissue mRNAs and in situ hybridization show that collagen XXIV is a product of cartilage, retina, cornea and skin. These are tissues where collagen fibril diameters are limited. From analysis of the sequence and the tissue distribution, we hypothesize that (i) type XXIV is a fibrillar collagen, and that (ii) it belongs in the subfamily of fibrillar collagens containing types V and XI. Because collagens V and XI are regulators of fibril diameter, we further hypothesize that (iii) collagen XXIV also functions to control fibril diameter.

L18 ANSWER 28 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2002098980 EMBASE <<LOGINID::20071018>>
TI SMIF, a Smad4-interacting protein that functions as a co-activator in TGF.beta. signalling.
AU Bai R.-Y.; Koester C.; Ouyang T.; Hahn S.A.; Hammerschmidt M.; Peschel C.; Duyster J.
CS J. Duyster, Department of Internal Medicine III, Laboratory of Leukemogenesis, Technical University of Munich, Ismaningerstrasse 22, 81675 Munich, Germany. justus.duyster@lrz.tum.de

SO Nature Cell Biology, (2002) Vol. 4, No. 3, pp. 181-190.
Refs: 50
ISSN: 1465-7392 CODEN: NCBIFN
CY United Kingdom
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 28 Mar 2002
Last Updated on STN: 28 Mar 2002
AB Proteins of the transforming growth factor .beta. (TGF.beta.) superfamily regulate diverse cellular responses, including cell growth and differentiation. After TGF.beta. stimulation, receptor-associated Smads are phosphorylated and form a complex with the common mediator Smad4. Here, we report the cloning of SMIF, a ubiquitously expressed, Smad4-interacting transcriptional co-activator. SMIF forms a TGF.beta./bone morphogenetic protein 4 (BMP4)-inducible complex with Smad4, but not with others Smads, and translocates to the nucleus in a TGF.beta./BMP4-inducible and Smad4-dependent manner. SMIF possesses strong intrinsic TGF.beta.-inducible transcriptional activity, which is dependent on Smad4 in mammalian cells and requires p300/CBP. A point mutation in Smad4 abolished binding to SMIF and impaired its activity in transcriptional assays. Overexpression of wild-type SMIF enhanced expression of TGF.beta./ ***BMP*** regulated genes, whereas a dominant-negative SMIF mutant suppressed expression. Furthermore, dominant-negative SMIF is able to block TGF.beta.-induced growth inhibition. In a knockdown approach with morpholino-antisense oligonucleotides targeting zebrafish SMIF, severe but distinct phenotypic defects were observed in zebrafish embryos. Thus, we propose that SMIF is a crucial activator of TGF.beta. signalling.

L18 ANSWER 29 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2002158792 EMBASE <<LOGINID::20071018>>
TI Studies of mechanism of guided bone regeneration by membrane technique.
AU Zhang Y.-G.; Lu S.-B.
CS Y.-G. Zhang, Department of Orthopedics, General Hospital of Chinese PLA, Beijing 100853, China
SO Chinese Journal of Biomedical Engineering, (2002) Vol. 21, No. 2, pp. 128-131.
Refs: 8
ISSN: 0258-8021 CODEN: ZSYXEI
CY China
DT Journal; Article
FS 021 Developmental Biology and Teratology
027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
005 General Pathology and Pathological Anatomy
LA Chinese
SL English; Chinese
ED Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002
AB A study of the mechanism of guided bone regeneration combined with osteoinduction by observation of histology and expressions of ***BMP*** , TGF-.beta., bFGF was carried ***ant*** . Adult male New Zealand rabbits were used for this purpose, and 10mm standard bone defect model was produced bilaterally in the middle radial shaft of each rabbit. Randomly, the defect on one side was enveloped with silicon membrane served as the test side, and the another unenveloped as a control. The animals were sacrificed at different time after surgery for histological observation, immunohistochemical staining of ***BMP*** , TGF-.beta. bFGF and in situ hybridization with cDNA probes. Results: (1)Histological finding of bone defects sealed by silicon membrane, showed inflammatory tissue and callus formed from cells in bony defects. (2) The expressions of ***BMP*** , TGF-.beta. and bFGF were similar between the test and control groups. (3) The total content of ***BMP*** , TGF-.beta., bFGF of all test sides was much higher than that of control sides (P<0.01). Conclusion: The key reason for successful guided bone regeneration is that membrane tube formed a relatively independent bone regenerative situation to prevent near-by tissue from inteference, and to prevent osteoinductors from diffusion, thus enhancing osteoinductors and inducing bone regeneration and repairing.

L18 ANSWER 30 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2003:324910 BIOSIS <<LOGINID::20071018>>
DN PREV200300324910
TI IDENTIFICATION AND CHARACTERIZATION OF A NOVEL NEURAL - SPECIFIC PROTEIN FAMILY, BRINP.
AU Matsuoka, I. [Reprint Author]; Nakatani, T. [Reprint Author]; Toda, F. [Reprint Author]; Ueno, S. [Reprint Author]; Mori, T. [Reprint Author]
CS Lab. Neurosci. Grad. Sch. Pharm. Sci., Hokkaido Univ., Sapporo, Japan
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 627.13. http://sfn.scholarone.com. cd-rom. Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 16 Jul 2003
Last Updated on STN: 16 Jul 2003
AB Bone morophogenetic protein (***BMP***) and retinoic acid (RA) play important roles in differentiation of nerve cells. We have previously shown that BMP2 and RA synergistically act on developing sympathetic neurons to induce their responsiveness to neurotrophic factors acting at the initial stage of development of these neurons. In an effort to clarify the mechanism of the actions of ***BMP*** /RA, we have identified BRINP1 (***BMP*** /RA-inducible neural-specific protein-1, 760 aa) whose expression is restricted to nervous system. In the present study, we identified two BRINP1-homologues, which comprise BRINP family. By screening of rat hippocampus cDNA library, we obtained two cDNA clones (4.1 and 3.0 kb) that are encoding proteins with total amino acid residues of 783 (BRINP2) and 766 (BRINP3), respectively. BRINP2 and BRINP3 have amino acid identity of 70% and both have amino acid identity of 50-53% with BRINP1. Like BRINP1, BRINP2 and BRINP3 have no conserved motifs except for a N-terminal ***signal*** ***peptide*** and a coiled-coil domain. Northern blot and Western blot analysis indicated that both BRINP2 and BRINP3 are predominantly expressed in the nervous system from developmental stage to adulthood. However, individual BRINP gene seems to have distinct regulatory mechanism of expression within the nervous system. In sympathetic neurons, BRINP1 expression was induced by ***BMP*** and RA, while BRINP2 and BRINP3 expressions were suppressed by these factors. In adult brains three BRINPs are expressed in partly overlapping and partly complementary manners. We are currently producing mice lacking BRINP family genes to clarify their physiological functions.

L18 ANSWER 31 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2001053155 EMBASE <<LOGINID::20071018>>
TI Cellular and molecular responses of the uterus to embryo implantation can be elicited by locally applied growth factors.
AU Paria B.C.; Ma W.-G.; Tan J.; Raja S.; Das S.K.; Dey S.K.; Hogan B.L.M.
CS B.L.M. Hogan, Howard Hughes Medical Institute, Department of Cell Biology, Vanderbilt Medical School, Nashville, TN 37232-2175, United States. brigid.hogan@mcmail.vanderbilt.edu
SO Proceedings of the National Academy of Sciences of the United States of America, (30 Jan 2001) Vol. 98, No. 3, pp. 1047-1052.
Refs: 36
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 021 Developmental Biology and Teratology
LA English
SL English
ED Entered STN: 16 Mar 2001
Last Updated on STN: 16 Mar 2001
AB The implantation of a blastocyst into a receptive uterus is associated with a series of events, namely the attachment reaction followed by decidualization of the stroma. Previous studies established that the gene encoding heparin-binding EGF-like growth factor (HB-EGF) is expressed in the luminal epithelium solely at the site of blastocyst apposition preceding the attachment reaction. We report here the expression during implantation of 21 genes encoding other signaling proteins, including those belonging to the Bone morphogenetic protein (***BMP***), fibroblast growth factor (FGF), WNT, and Hedgehog (HH) pathways. We find that the attachment reaction is associated with a localized stromal induction of genes encoding ***BMP*** -2, FGF-2, and WNT-4. Despite efforts by many investigators, a simple in vitro model of implantation is not yet available to study either the hierarchy of the events triggered in the uterus by the embryo or the function of individual signaling proteins. We have therefore approached these questions by introducing beads loaded with purified factors into the receptive uterus. We show that beads soaked in HB-EGF or insulin-like growth factor-1 (IGF-I), but not other proteins, induce many of the same discrete local responses elicited by the blastocyst, including increased localized vascular permeability, decidualization, and expression of Bmp2 at the sites of the beads. By contrast, the expression domains of Indian hedgehog (Ihh), patched, and noggin become restricted as decidualization proceeds. Significantly, beads containing ***BMP*** -2 do not themselves elicit an implantation response but affect the spacing of implantation sites induced by blastocysts cotransferred with the beads.

L18 ANSWER 32 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
AN 2001:59288 BIOSIS <<LOGINID::20071018>>
DN PREV200100059288
TI An Epstein-Barr virus protein interacts with Notch.
AU Kusano, Shuichi; Raab-Traub, Nancy [Reprint author]
CS Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC, 27599-7295, USA nrt@med.unc.edu
SO Journal of Virology, (January, 2001) Vol. 75, No. 1, pp. 384-395. print. CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
ED Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002
AB The Epstein-Barr virus (EBV) BamHI A mRNAs were originally identified in cDNA libraries from nasopharyngeal carcinoma, where they are expressed at high levels. The RNAs are differentially spliced to form several open reading frames and also contain the BARF0 open reading frame at the 3'

end. One cDNA, RKBARF0, included a potential endoplasmic reticulum-targeting ***signal*** ***peptide*** sequence. The RK-BARF0 protein is shown here to interact with the Notch4 ligand binding domain, using yeast two-hybrid screening, coimmunoprecipitation, and confocal microscopy. This interaction induces translocation of a portion of the full-length unprocessed Notch4 to the nucleus by using the Notch nuclear localization signal. These effects of RK-BARF0 on Notch intracellular location indicate that EBV possibly modulates Notch signaling. Unprocessed Notch4 was also detected in immunoprecipitated complexes from EBV-infected cells by using a rabbit antiserum raised against a BARF0-specific peptide. This finding provides additional evidence for expression of RK-BARF0 and its interaction with Notch during EBV infection. In EBV-infected, EBNA2-negative cells, RK-BARF0 induced the expression of EBV latent membrane protein 1 (***LMP1***), and this induction was dependent on the RK-BARF0/Notch interaction domain. The activation of ***LMP1*** expression by RK-BARF0 may be responsible for expression of ***LMP1*** in EBV latent infections in the absence of EBNA2.

L18 ANSWER 33 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2001266265 EMBASE <<LOGINID::20071018>>
TI Bone morphogenetic protein-2 (***BMP*** -2) signaling to the Col2.alpha.1 gene in chondroblasts requires the homeobox gene Dlx-2.
AU Xu S.C.; Harris M.A.; Rubenstein J.L.R.; Mundy G.R.; Harris S.E.
CS Dr. S.C. Xu, Procter And Gamble Pharmaceuticals, 8700 Mason-Montgomery Road, Mason, OH 45040, United States. xu.sc@pg.com
SO DNA and Cell Biology, (2001) Vol. 20, No. 6, pp. 359-365.
Refs: 26
ISSN: 1044-5498 CODEN: DCEBE8
CY United States
DT Journal; Article
FS 022 Human Genetics
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 16 Aug 2001
Last Updated on STN: 16 Aug 2001
AB To understand the role of Dlx genes in the process of chondrogenesis, we studied the expression of Dlx-2 and Dlx-5 mRNAs in a mouse clonal chondroblast cell line, TMC23. We also examined the involvement of Dlx2 in the bone morphogenetic protein-2 (***BMP*** -2) signaling to the type II collagen gene, Col2.alpha.1, in this cell line. In this report, we show that the TMC23 cells expresse Dlx-2 and Dlx-5 mRNAs, and the levels can be upregulated by recombinant ***BMP*** -2 at an early stage of chondroblast differentiation. Addition of rBMP-2 dramatically increased type II collagen expression at both the mRNA and the protein level. Also, rBMP-2 increased transcription of Col2.alpha.1, as shown by stimulation of a chondrocyte-specific Col2.alpha.1 enhancer. The mechanism involves Dlx-2, as the stimulatory effect of rBMP-2 on the Col2.alpha.1 enhancer was blocked by an antisense oligonucleotide against Dlx-2 mRNA. The rBMP-2 signaling to the Col2.alpha.1 enhancer was also blocked by a dominant-negative Smad1 expression vector. These data demonstrate that Dlx-2 is a downstream target of the ***BMP*** -2 signaling pathway in chondroblasts. Therefore, we propose a model in which rBMP-2 stimulates Dlx-2 expression, which then serves as a necessary transcription factor for Col2.alpha.1 gene expression through a chondrocyte-specific enhancer fragment.

L18 ANSWER 34 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 8
AN 2000:369710 BIOSIS <<LOGINID::20071018>>
DN PREV200000369710
TI MEPE, a new gene expressed in bone marrow and tumors causing osteomalacia.
AU Rowe, Peter S. N. [Reprint author]; de Zoysa, Priyal A.; Dong, Rong; Wang, Huei Rong; White, Kenneth E.; Econs, Michael J.; Oudet, Claudine L.
CS Centre for Molecular Osteo-Renal Research, Department of Biochemistry and Molecular Biology, Royal Free and University College Medical School, Rowland Hill Street, Hampstead, London, NW3 2PF, UK
SO Genomics, (July 1, 2000) Vol. 67, No. 1, pp. 54-68. print.
CODEN: GNMCEP. ISSN: 0888-7543.
DT Article
LA English
ED Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002
AB Oncogenic hypophosphatemic osteomalacia (OHO) is characterized by a renal phosphate leak, hypophosphatemia, low-serum calcitriol (1,25-vitamin-D3), and abnormalities in skeletal mineralization. Resection of OHO tumors results in remission of the symptoms, and there is evidence that a circulating phosphaturic factor plays a role in the bone disease. This paper describes the characterization and cloning of a gene that is a candidate for the tumor-secreted phosphaturic factor. This new gene has been named MEPE (matrix extracellular phosphoglycoprotein) and has major similarities to a group of bone-tooth mineral matrix phospho-glycoproteins (osteopontin (OPN; HGMW-approved symbol SPP1), dentin sialo phosphoprotein
(DSPP), dentin matrix protein 1 (DMP1), bone sialoprotein II (IBSP), and bone morphogenetic proteins (***BMP***). All the proteins including MEPE contain RGD sequence motifs that are proposed to be essential for integrin-receptor interactions. Of further interest is the finding that MEPE, OPN, DSPP, DMP1, IBSP, and BMP3 all map to a defined region in chromosome 4q. Refined mapping localizes MEPE to 4q21.1 between ESTs D4S2785 (WI-6336) and D4S2844 (WI-3770). MEPE is 525 residues in length with a short N-terminal ***signal*** ***peptide*** . High-level expression of MEPE mRNA occurred in all four OHO tumors screened. Three of 11 non-OHO tumors screened contained trace levels of MEPE expression (detected only after RT-PCR and Southern 32P analysis). Normal tissue expression was found in bone marrow and brain with very-low-level expression found in lung, kidney, and human placenta. Evidence is also presented for the tumor secretion of clusterin (HGMW-approved symbol CLU) and its possible role as a cytotoxic factor in one of the OHO patients described.

L18 ANSWER 35 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 9
AN 2001:27925 BIOSIS <<LOGINID::20071018>>
DN PREV200100027925
TI Overexpression of DAN causes a growth suppression in p53-deficient SAOS-2 cells.
AU Hanaoka, Eiji; Ozaki, Toshinori; Nakamura, Yohko; Moriya, Hideshige; Nakagawara, Akira; Sakiyama, Shigeru [Reprint author]
CS Division of Biochemistry, Chiba Cancer Center Research Institute, 666-2 Nitona, Chuoh-ku, Chiba, 260-8717, Japan
ssakiyam@chiba-cc.chiba.pref.jp
SO Biochemical and Biophysical Research Communications, (November 11, 2000)
Vol. 278, No. 1, pp. 20-26. print.
CODEN: BBRCA9. ISSN: 0006-291X.
DT Article
LA English
ED Entered STN: 10 Jan 2001
Last Updated on STN: 12 Feb 2002
AB It has been shown that the expression of DAN as well as Drm/Gremlin, a member of DAN/Cerberus family, is significantly down-regulated in rodent fibroblasts transformed with various oncogenes and overexpression of DAN results in the phenotypic reversion of the transformed phenotypes. In the present study, we examined the expression levels of DAN, ***BMP*** -2, ***BMP*** -4, and BMPRs (***BMP*** receptors) in five human cell lines derived from bone and soft tissue tumors. Northern blot analysis revealed that DAN mRNA was detected in OS-KH and RMS-NK cells, but was not
detectable in SAOS-2, NOS-1, and ASPS-KY cells. Transient overexpression of DAN in SAOS-2 cells, which lack functional p53 and pRB, resulted in a remarkable growth suppression without the induction of p21Waf1. Interestingly, overexpression of DAN was associated with a reduction of alkaline phosphatase activity in SAOS-2 cells. Stable transfection of DAN in SAOS-2 cells caused a significant reduction of numbers of drug-resistant colonies, whereas the truncated form of DAN which lacked a possible ***signal*** ***peptide*** , completely lost this capability. Our results suggest that the secreted form of DAN exerts its growth-suppressive function in SAOS-2 cells in a p53-independent manner.

L18 ANSWER 36 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1999194734 EMBASE <<LOGINID::20071018>>
TI Noggin expression in a mesodermal pluripotent cell line C1 and its regulation by ***BMP*** .
AU Nifuji A.; Kellermann O.; Noda M.
CS M. Noda, Department of Molecular Pharmacology, Medical Research Institute, Tokyo Medical and Dental University, 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo 101-0062, Japan
SO Journal of Cellular Biochemistry, (15 Jun 1999) Vol. 73, No. 4, pp. 437-444.
Refs: 32
ISSN: 0730-2312 CODEN: JCEBD5
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
LA English
SL English
ED Entered STN: 1 Jul 1999
Last Updated on STN: 1 Jul 1999
AB Osteoblasts and chondrocytes are derived from mesodermal stem cells and their differentiation is under the control of coordinated interaction among signaling molecules. Noggin is one of the signaling molecules which bind to and inactivate BMPs to induce neural tissues and dorsal mesoderm in Xenopus. However, its expression and regulation in mammalian cells has not been known. In this study, we investigated expression of noggin in murine pluripotent mesodermal cell line, C1. Noggin expression was very low in these C1 cells before they were induced to differentiate. When C1 cells were induced to differentiate into chondrocytes in aggregate cultures in the presence of dexamethasone(dex), noggin expression was significantly increased. In a sharp contrast, when the C1 cells were induced to differentiate into osteoblastic cells by the treatment with .beta. glycerophosphate (.beta.GP) and ascorbic acid (AA), noggin mRNA expression remained to be barely detectable. Noggin expression was also observed in the developing cartilage of vertebrae in 15.5 dpc mouse embryos. The noggin mRNA level in C1 cells in monolayer cultures was enhanced significantly by the treatment with BMP4/7 in a dose-dependent manner with a maximal effect at 100 ng/ml. The BMP4/7 effect on noggin expression was time dependent starting within 12 h and peaked at 24 h. These results indicate that noggin is expressed in the pluripotent

mesodermal cell line C1 and that its expression is regulated by ***BMP*** .

L18 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:562595 CAPLUS <<LOGINID::20071018>>
DN 131:320517
TI Hensin, the polarity reversal protein, is encoded by DMBT1, a gene frequently deleted in malignant gliomas
AU Takito, Jiro; Yan, Lunbiao; Ma, Jian; Hikita, Chinami; vijayakumar, S.; Warburton, D.; Al-Awqati, Qais
CS College of Physicians and Surgeons, Columbia University, New York, NY, 10032, USA
SO American Journal of Physiology (1999), 277(2, Pt. 2), F277-F289
CODEN: AJPHAP; ISSN: 0002-9513
PB American Physiological Society
DT Journal
LA English
AB The band 3 anion exchanger is located in the apical membrane of a .beta.-intercalated clonal cell line, whereas the vacuolar H+-ATPase is present in the basolateral membrane. When these cells were seeded at confluent d., they converted to an .alpha.-phenotype, localizing each of these proteins to the opposite cell membrane domain. The reversal of polarity is induced by hensin, a 230-kDa extracellular matrix protein. Rabbit kidney hensin is a multi-domain protein composed of eight SRCR ("scavenger receptor, cysteine rich"), two CUB ("C1r/C1s Uegf ***Bmp*** 1"), and one ZP ("zona pellucida") domain. Other proteins known to have these domains include CRP-ductin, a cDNA expressed at high levels in mouse intestine (8 SRCR, 5 CUB, 1 ZP), ebnerin, a protein cloned from a rat taste bud library (4 SRCR, 3 CUB, 1 ZP), and DMBT1, a sequence in human chromosome 10q25-26 frequently deleted in malignant gliomas (9 SRCR, 2 CUB, 1 ZP). Rabbit and mouse hensin genomic clones contained a new SRCR that was not found in hensin cDNA but was homologous to the first SRCR domain in DMBT1. Furthermore, the 3'-untranslated regions and the ***signal*** ***peptide*** of hensin were homologous to those of DMBT1. Mouse genomic hensin was localized to chromosome 7 band F4, which is syntenic to human 10q25-26. These data suggest that hensin and DMBT1 are alternatively spliced forms of the same gene. The anal. of mouse hensin bacterial artificial chromosome (BAC) genomic clone by sequencing and Southern hybridization revealed that the gene also likely encodes CRP-ductin. A new antibody against the mouse SRCR1 domain recognized a protein in the mouse and rabbit brain but not in the immortalized cell line or kidney, whereas an antibody to SRCR6 and SRCR7 domains which are present in all the transcripts, recognized proteins in intestine, kidney, and brain from several species. The most likely interpretation of these data is that one gene produces at least three transcripts, namely, hensin, DMBT1, and CRP-ductin. Hensin may participate in detg. the polarized phenotype of other epithelia and brain cells.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:803928 CAPLUS <<LOGINID::20071018>>
DN 130:62035
TI sequence and functional expression and therapeutic applications for human chordin
IN Lavallie, Edward R.; Racie, Lisa A.; Derobertis, Edward M.
PA Genetics Institute, Inc., USA
SO U.S., 22 pp., Cont.-in-part of U.S. 5,679,783.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5846770	A	19981208	US 1996-749169	19961114
US 5679783	A	19971021	US 1994-343760	19941122
WO 9821335	A1	19980522	WO 1997-US18151	19971007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9748960	A	19980603	AU 1997-48960	19971007
US 5986056	A	19991116	US 1998-130032	19980804
PRAI US 1994-343760	A2	19941122		
US 1996-749169	A	19961114		
WO 1997-US18151	W	19971007		

AB Purified chordin proteins and processes for producing them are disclosed which include construction of chimeric proteins utilizing the TGF-.beta. ***signal*** ***peptide*** . DNA mols. encoding the chordin proteins are also disclosed. The proteins may be used in the treatment of bone, cartilage, other connective tissue defects and disorders, including tendon, ligament and meniscus, in wound healing and related tissue repair, as well as for treatment of disorders and defects to tissues which include epidermis, nerve, muscle, including cardiac muscle, and other tissues and wounds, and organs such as liver, brain, lung, cardiac, pancreas and kidney tissue. The proteins may also be useful for the induction inhibition of growth and/or differentiation of undifferentiated embryonic and stem cells. The proteins may be complexed with other proteins, particularly members of the transforming growth factor-beta superfamily of proteins. These proteins may be used for augmenting the activity of bone morphogenic proteins.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:236561 CAPLUS <<LOGINID::20071018>>
DN 128:253812
TI Cloning, expression and production of tasty peptides
IN Lerch, Konrad; Muheim, Andreas; Silke, Natasha
PA Givaudan-Roure (International) S.A., Switz.
SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 832972	A2	19980401	EP 1997-116132	19970917
EP 832972	A3	19991117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 10108686	A	19980428	JP 1997-242596	19970908
PRAI EP 1996-115211	A	19960923		

AB The present invention relates to organisms comprising tasty peptides or parts or exts. thereof, the prodn. of tasty peptides in organisms via recombinant expression of said tasty peptides. Three specific peptides are disclosed: a beefy meaty peptide (***BMP*** , Lys-Gly-Asp-Glu-Glu-Ser-Leu-ALA), a cheese tasty peptide (Asp-Lys-Ile-His-Pro-Phe), and a bitter tasting peptide (Arg-Gly-Pro-Phe-Ile-Ile-Val). Organisms comprising tasty peptides or parts or exts. thereof, tasty peptides in homogeneous form, DNA sequences encoding these peptides and vectors contg. these DNA sequences are provided, along with methods for recombinantly producing such peptides, DNA sequences, vectors and organisms. Four different recombinant techniques are described: (1) synthetic oligonucleotide ligation and insertion into the expression vector pMal-C2 for prodn. as a fusion protein with maltose-binding protein in Escherichia coli, (2) fusion to the .alpha.-factor signal protein in the pNS2 plasmid for transformation and expression in Saccharomyces cerevisiae, (3) expression as tandem repeats in yeast, each repeat preceded by a short spacer peptide (Lys-Arg-Glu-Ala-Glu-Ala), and (4) expression of repetitive artificial proteins comprising the peptide repeatedly. The peptides have value for food applications in isolated form or as the recombinant food-grade microorganism.

L18 ANSWER 40 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1996373617 EMBASE <<LOGINID::20071018>>
TI Epstein-Barr virus ***LMP1*** induction of the epidermal growth factor receptor is mediated through a TRAF signaling pathway distinct from NF-.kappa.B activation.
AU Miller W.E.; Mosialos G.; Kieff E.; Raab-Traub N.
CS N. Raab-Traub, Dept. of Microbiology and Immunology, Lineberger Comprehensive Can. Ctr., Univ. of North Carolina Sch. of Med., Chapel Hill, NC 27599, United States
SO Journal of Virology, (1997) Vol. 71, No. 1, pp. 586-594.
Refs: 68
ISSN: 0022-538X CODEN: JOVIAM
CY United States
DT Journal; Article
FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 25 Jan 1997
Last Updated on STN: 25 Jan 1997
AB The Epstein-Barr virus (EBV)-encoded ***LMP1*** protein induces several cellular changes including induction of epidermal growth factor receptor (EGFR) expression and activation of the NF-.kappa.B transcription factor. Two domains within the carboxy terminus have been identified that activate NF- .kappa.B. In this study, mutational analysis of the ***LMP1*** protein indicated that the proximal NF-.kappa.B activation domain, which is identical to the TRAF interaction domain (amino acids 187 to 231), is essential for induction of the EGFR. The distal NF-.kappa.B activation domain (amino acids 352 to 386) did not induce expression of the EGFR. In contrast, the two domains both independently activated a .kappa.B-CAT reporter gene and induced expression of the NF-.kappa.B-regulated A20 gene in C33A epithelial cells. These results indicate that induction of the EGFR by ***LMP1*** involves the TRAF interaction domain and that activation of NF-.kappa.B alone is not sufficient. Northern blot analysis revealed that induction of EGFR and A20 expression is likely to be at the transcriptional level. Interestingly expression of CD40 in the C33A cells also induced expression of the EGFR. Overexpression of either TRAF3 or an amino-terminal-truncated form of TRAF3 (TRAF3-C) inhibited signaling from the ***LMP1*** TRAF interaction domain but did not affect signaling from the distal NF- .kappa.B activation domain. These data further define the mechanism by which ***LMP1*** induces expression of the EGFR and indicate that TRAF signaling from ***LMP1*** and CD40 activates a downstream transcription pathway distinct from NF-.kappa.B that induces

expression of the EGFR.

L18 ANSWER 41 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1997084008 EMBASE <<LOGINID::20071018>>
TI XBMP-1B (Xtld), a Xenopus homolog of dorso-ventral polarity gene in Drosophila, modifies tissue phenotypes of ventral explants.
AU Lin J.-J.; Maeda R.; Ong R.C.; Kim J.; Lee L.M.; Kung H.-F.; Maeno M.
CS M. Maeno, Department of Biology, Faculty of Science, Niigata University, Niigata 950-21, Japan
SO Development Growth and Differentiation, (1997) Vol. 39, No. 1, pp. 43-51.
Refs: 30
ISSN: 0012-1592 CODEN: DGDFA5
CY Japan
DT Journal; Article
FS 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
AB Previously we have isolated a Xenopus cDNA homolog of bone morphogenetic
protein-1 (XBMP-1A). In the present report we describe a new cDNA clone called XBMP-1B (or Xtld) from a Xenopus embryonic library. Sequence analysis indicates that these two clones share an identical N-terminal sequence, including a region of metalloprotease domain, three copies of a repeat first found in complement proteins Clr/s and an epidermal growth factor (EGF)-like sequence, XBMP-1 B protein has an additional copy of an EGF-like sequence followed by two copies of complement 1 r/s repeat in the C-terminus. The overall protein structure predicted from the XBMP-1B sequence reveals that it encodes a protein homologous to Drosophila tolloid. Three XBMP-1 transcripts (2.9, 5.2 and 6.6 kb) were detected by northern blot analysis. However, the 2.9 kb transcript hybridized specifically with XBMP-1A and the 5.2 and 6.6 kb transcripts hybridized with XBMP-1B. In Drosophila, a major function of tolloid is to augment the activity of the decapentaplegic gene product, a close relative of tumor growth factor (TGF)-.beta. superfamily members, ***BMP*** -2/4. Although XBMP-1 and XBMP-4 are detected in various adult tissues of Xenopus, the expression pattern of these two genes was not tightly correlated. In the embryo, the expression of XBMP-1 increased gradually from the morula to the swimming tadpole stages. Injection of XBMP1B RNA into the ventral blastomeres at the 4-cell stage caused an elongation of the ventral marginal zone explants and converted globin-positive blood cells to mesenchymal and muscle tissues at later stages. It was shown that XBMP-1A was less active and a 1A mutant lacking the signal sequence was inactive. Further studies revealed that injection of XBMP-1B RNA into the ventral marginal zone induced up- regulation of dorsal marginal zone markers, such as goosecoid and chordin, at the gastrulation stage. These data indicate that XBMP-1 may have a role in determining dorso- ventral patterning in Xenopus, but in a different way from the dpp/tolloid system demonstrated in Drosophila.

L18 ANSWER 42 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1995006328 EMBASE <<LOGINID::20071018>>
TI A 135-kilodalton surface antigen of Mycoplasma hominis PG21 contains multiple directly repeated sequences.
AU Ladefoged S.A.; Birkelund S.; Hauge S.; Brock B.; Jensen L.T.; Christiansen G.
CS S.A. Ladefoged, Medical Microbiology/Immunol. Dept., Bartholin Building, University of Aarhus, DK-8000 Aarhus C, Denmark
SO Infection and Immunity, (1995) Vol. 63, No. 1, pp. 212-223.
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 25 Jan 1995
Last Updated on STN: 25 Jan 1995
AB A monoclonal antibody was used to characterize a 135-kDa surface-located membrane protein (***Lmp1***) generally present in Mycoplasma hominis strains. The monoclonal antibody, 552, was applied to identify the corresponding gene in an expression library of M. hominis PG21 DNA. The M. hominis PG21 ***lmp1*** gene was sequenced, and its gene product was characterized with the goal of elucidating the structure and function of ***Lmp1*** . A total of 7,196 bp in the ***lmp1*** region was sequenced. An open reading frame of 4,032 bp, encoding a protein of 1,344 amino acids with a calculated molecular weight of 147,000, was identified. Analysis of the deduced amino acid sequence predicted a hydrophilic protein with a basic pI (10.0). The N-terminal 24 amino acids were a typical leader sequence. Downstream from the first 726 nucleotides, six similar direct repeats of 471 nucleotides were found. In repeat 7, a single-base substitution, C.fwdarw.A, gave rise to the stop codon of ***lmp1*** . Thus, the C-terminal 945 amino acids were encoded by the 471-bp direct repeats. As evidenced by Southern blot analysis, the gene encoding the 135-kDa antigen is part of a multigene family. One of the genes, lmp2, was situated directly downstream from ***lmp1*** where the direct repeats continued.

L18 ANSWER 43 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1994372666 EMBASE <<LOGINID::20071018>>
TI The Spi-1/PU.1 and Spi-B ets family transcription factors and the recombination signal binding protein RBP-J.kappa. interact with an Epstein-Barr virus nuclear antigen 2 responsive cis-element.
AU Laux G.; Adam B.; Strobl L.J.; Moreau-Gachelin F.
CS G. Laux, Inst Klin Molekularbiol Tumorgenetik, GSF-Forschungszentrum, Umwelt und Gesundheit GmbH, Marchioninistrasse 25, D-81377 Munchen, Germany
SO EMBO Journal, (1 Dec 1994) Vol. 13, No. 23, pp. 5624-5632.
Refs: 63
ISSN: 0261-4189 CODEN: EMJODG
CY United Kingdom
DT Journal; Article
FS 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 29 Dec 1994
Last Updated on STN: 29 Dec 1994
AB Epstein-Barr virus (EBV) immortalizes resting human B cells very efficiently in vitro. The EBV nuclear protein EBNA2 is absolutely required for this process. It also activates transcription of cellular, as well as viral, genes. It is assumed that EBNA2 contributes to B cell immortalization by its transactivating potential, since its transforming and transactivating functions could not be separated. Mutational analysis of the 80 bp EBNA2 responsive cis-element within the viral bidirectional ***LMP*** /TP2 promoter region identified two sequence elements, which are both essential for transactivation by EBNA2. These sequences harbour putative consensus binding sites for Spi-1 oncoprotein and recombination signal binding protein RBP-J.kappa., the homologue of Drosophila Suppressor of Hairless. Electrophoretic mobility shift assays demonstrated the high affinity binding of Spi-1 and Spi-B, both members of the Ets family of transcription factors, to one sequence element. The other element bound RBP-.kappa. with low affinity. In addition, co-transfections showed that the replacement of the Spi-1/Spi-B binding site in the bi-directional ***LMP*** /TP2 promoter by the analogous SV40 Spi-1 responsive element did not impair its function on EBNA2-mediated transactivation. It is concluded that the transcriptional regulators Spi-1 and Spi-B as well as RBP-.kappa. play an essential role in transactivating the ***LMP*** /TP2 promoter by EBNA2 and therefore in the immortalization of B cells by EBV.

L18 ANSWER 44 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1994182592 EMBASE <<LOGINID::20071018>>
TI Expression and growth inhibitory effect of decapentaplegic Vg-related protein 6: Evidence for a regulatory role in keratinocyte differentiation.
AU Drozdoff V.; Wall N.A.; Pledger W.J.
CS V. Drozdoff, Department of Cell Biology, Vanderbilt Univ. School of Medicine, Nashville, TN 37232, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (7 Jun 1994) Vol. 91, No. 12, pp. 5528-5532.
Refs: 31
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 6 Jul 1994
Last Updated on STN: 6 Jul 1994
AB Decapentaplegic Vg-related protein 6 (DVR-6 or bone morphogenetic protein ***BMP*** -6) is a member of the DVR subgroup of the transforming growth factor .beta. superfamily, a large group of multifunctional signaling polypeptides that are expressed as secreted disulfide-bonded dimers proteolytically cleaved from larger precursors. The predominant expression of DVR-6 in the differentiating postmitotic layers of stratified squamous epithelia strongly suggests a role for DVR-6 in regulation of epithelial differentiation. In primary mouse keratinocytes induced to differentiate by suspension culture in methylcellulose, new expression of DVR-6 mRNA and protein was detected within 8 h among a majority of the suspended cells, which preceded the induction of expression of the suprabasal keratins K1 and K10. To test the hypothesis that DVR-6 is a keratinocyte growth regulatory factor, a retroviral expression vector expressing human DVR-6 was used to infect attached cultures of undifferentiated basal cells. Expression of DVR-6 in primary mouse keratinocytes before differentiation resulted in the secretion of prepro and processed (pro region) forms in the conditioned medium and a dramatic inhibition of cell growth. These findings suggest that inhibition of cell growth by DVR-6 may be a primary step in keratinocyte differentiation.

L18 ANSWER 45 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1995007621 EMBASE <<LOGINID::20071018>>
TI Sonic hedgehog and Fgf-4 act through a signaling cascade and feedback loop to integrate growth and patterning of the developing limb bud.
AU Laufer E.; Nelson C.E.; Johnson R.L.; Morgan B.A.; Tabin C.
CS E. Laufer, Department of Genetics, Harvard Medical School, Boston, MA 02115, United States
SO Cell, (1994) Vol. 79, No. 6, pp. 993-1003.
Refs: 49
ISSN: 0092-8674 CODEN: CELLB5

CY United States
DT Journal; Article
FS 021 Developmental Biology and Teratology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 25 Jan 1995
Last Updated on STN: 25 Jan 1995
AB Proper limb growth and patterning requires signals from the zone of polarizing activity in the posterior mesoderm and from the overlying apical ectodermal ridge (AER). Sonic hedgehog and Fgf-4, respectively, have recently been identified as candidates for these signals. We have dissected the roles of these secreted proteins in early limb development by ectopically regulating their activities in a number of surgical contexts. Our results indicate that Sonic hedgehog initiates expression of secondary signaling molecules, including ***Bmp*** -2 in the mesoderm and Fgf-4 in the ectoderm. The mesoderm requires ectodermally derived competence factors, which include Fgf- 4, to activate target gene expression in response to Sonic hedgehog. The expression of Sonic hedgehog and Fgf-4 is coordinately regulated by a positive feedback loop operating between the posterior mesoderm and the overlying AER. Taken together, these data provide a basis for understanding the integration of growth and patterning in the developing limb.

L18 ANSWER 46 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1994246873 EMBASE <<LOGINID::20071018>>
TI Characterization and relationship of dpp receptors encoded by the saxophone and thick veins genes in Drosophila.
AU Brummel T.J.; Twombly V.; Marques G.; Wrana J.L.; Newfeld S.J.; Attisano L.; Massague J.; O'Connor M.B.; Gelbart W.M.
CS T.J. Brummel, Molecular Biol./Biochemistry Dept., University of California, Irvine, CA 92717, United States
SO Cell, (1994) Vol. 78, No. 2, pp. 251-261.
Refs: 48
ISSN: 0092-8674 CODEN: CELLB5
CY United States
DT Journal; Article
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 31 Aug 1994
Last Updated on STN: 31 Aug 1994
AB The dpp/ ***BMP*** family of TGF.beta.-related factors controls numerous events in pattern formation and morphogenesis. How these polypeptide signals are received and transduced by target cells is largely unknown. We combine molecular and genetic approaches to establish that the Drosophila saxophone (sax) gene encodes a dpp receptor. We compare the structural properties and expression patterns of sax with a second dpp receptor encoded by the thick veins (tkv) gene. While the sax gene is expressed ubiquitously, tkv is expressed in a highly localized and dynamic pattern during development. Some, but not all, of the tkv expression pattern parallels that of dpp. Ubiquitous expression of a tkv transgene rescues both tkv and sax loss-of-function mutations. Thus, there is at least partial functional overlap of the sax and tkv receptors in vivo. We consider these observations in terms of possible ligand-receptor interactions during Drosophila development.

L18 ANSWER 47 OF 51 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1994030243 EMBASE <<LOGINID::20071018>>
TI What do BMPs do in mammals? Clues from the mouse short-ear mutation.
AU Kingsley D.M.
CS D.M. Kingsley, Dept. Developmental Biology, Beckman Center B300, Stanford University School Medicine, Stanford, CA 94305-5427, United States
SO Trends in Genetics, (1994) Vol. 10, No. 1, pp. 16-21.
Refs: 39
ISSN: 0168-9525 CODEN: TRGEE2
CY United Kingdom
DT Journal; General Review; (Review)
FS 021 Developmental Biology and Teratology
022 Human Genetics
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 27 Feb 1994
Last Updated on STN: 27 Feb 1994
AB Bone morphogenetic proteins (BMPs) are a family of secreted signaling molecules that were oiginally isolated on the basis of their remarkable ability to induce the formation of ectopic bones when implanted into adult animals. The first mutations identified in a mammalian ***BMP*** gene suggest that members of this family induce the formation, patterning and repair of particular morphological features in higher animals.

L18 ANSWER 48 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 1993:275169 BIOSIS <<LOGINID::20071018>>
DN PREV199396005394
TI Structural analysis of a protein component of the black widow spider venom interacting with alpha-latrotoxin.
AU Kiyatkin, N. I.; Dulubova, I. E.; Volkova, T. M.; Chekhovskaya, I. A.; Lipkin, A. V.; Grishin, E. V.
CS M.M. Shemyakin Inst. Bioorg. Chem., Acad. Sci. Russ., Moscow, Russia
SO Doklady Akademii Nauk, (1992) Vol. 323, No. 1, pp. 178-180.
DT Article
LA Russian
ED Entered STN: 9 Jun 1993
Last Updated on STN: 9 Jun 1993
AB Cloning and structural analysis of low molecular weight protein (***LMP***) from the venom of Latrodectus mactans tredecimguttatus were carried out. This protein is coreleased with alpha latrotoxin. The structure of the encoding cDNA chain is described as is the corresponding amino acid sequence of ***LMP*** . The analysis of this sequence shows that ***LMP*** is synthesized as a protein precursor which consists of a ***signal*** ***peptide*** containing 18 amino acid residues, and the protein itself consisting of 70 amino acid residues.

L18 ANSWER 49 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 10
AN 1992:209132 BIOSIS <<LOGINID::20071018>>
DN PREV199293109357; BA93:109357
TI SPATIAL AND TEMPORAL EXPRESSION PATTERN DURING SEA URCHIN EMBRYOGENESIS OF
A GENE CODING FOR A PROTEASE HOMOLOGOUS TO THE HUMAN PROTEIN ***BMP***
-1 AND TO THE PRODUCT OF THE DROSOPHILA DORSAL-VENTRAL PATTERNING GENE
TOLLOID.
AU LEPAGE T [Reprint author]; GHIGLIONE C; GACHE C
CS UNITE BIOLOGIE CELLULAIRE MARINE, CENT NATIONAL RECHERCHE SCIENTIFIQUE,
UNIV PARIS VI, STATION MARINE, 06230 VILLEFRANCHE-SUR-MER, FR
SO Development (Cambridge), (1992) Vol. 114, No. 1, pp. 147-163.
CODEN: DEVPED. ISSN: 0950-1991.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 4 May 1992
Last Updated on STN: 1 Jun 1992
AB A cDNA clone coding for a sea urchin embyronic protein was isolated from a prehatching blastula .lambda.gt11 library. The predicted translation product is a secreted 64 .times. 103 Mr enzyme designated as BP10. The protein contains several domains: a ***signal*** ***peptide*** , a putative propeptide, a catalytic domain with an active center typical of a Zn2+-metalloprotease, an EGF-like domain and two internal repeats similar to repeated domains found in the C1s and C1r serine proteases of the complement cascade. The BP10 protease is constructed with the same domains as the human bone morphogenetic protein ***BMP*** -1, a protease described as a factor involved in bone formation, and as the recently characterized product of the tolloid gene which is required for correct dorsal-ventral patterning of the Drosophila embryo. The transcription of the BP10 gene is transiently activated around the 16- to 32-cell stage and the accumulation of BP10 transcripts is limited to a short period at the blastula stage. By in situ hybridization with digoxgenin-labelled RNA probes, the BP10 transcripts were only detected in a limited area of the blastula, showing that the transcription of the BP10 gene is also spatially controlled. Antibodies directed against a fusion protein were used to detect the BP10 protein in embryonic extracts. The protein is first detected in early blastula stages, its levels peaks in late cleavage, declines abruptly before ingression of primary mesenchyme cells and remains constant in late development. The distribution of the BP10 protein during its synthesis and secretion was analysed by immunostaining blastula-stage embryos. The intracellular localization of the BP10 staining varies with time. The protein is first detected in a perinuclear region, then in an apical and submembranous position just before its secretion into the perivitelline space. The protein is synthesized in a sharply delimited continuous territory spanning about 70% of the blastula. Comparison of the size and orientation of the labelled territory in the late blastula with the fate map of the blastula stage embryo shows that the domain in which the BP10 gene is expressed corresponds to the presumptive ectoderm. Developing embryos treated with purified antibodies against the BP10 protein and with synthetic peptides derived from the EGF-like domain displayed perturbations in morphogenesis and were radialized to various degrees. These results are consistent with a role for BP10 in the differentiation of ectodermal lineages and subsequent patterning of the embryo. On the basis of these results, we speculate that the role of BP10 in the sea urchin embryo might be similar to that of tolloid in Drosophila. We discuss the idea that the processes of saptial regulation of gene expression along the animal-vegetal in sea urchin and dorsal-ventral axes in Drosophila might have some similarities and might use common elements.

L18 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1993:188065 CAPLUS <<LOGINID::20071018>>
DN 118:188065
TI Spatial and temporal expression pattern during sea urchin embryogenesis of a gene coding for a protease homologous to the human protein ***BMP*** -1 and to the product of the Drosophila dorsal-ventral patterning gene tolloid
AU Lepage, Thierry; Ghiglione, Christian; Gache, Christian
CS Unite Biol. Cell. Mar., Univ. Paris VI, Villefranche-sur-Mer, 06230, Fr.
SO Development (Cambridge, United Kingdom) (1992), 114(11), 147-63, 2 plates
CODEN: DEVPED; ISSN: 0950-1991
DT Journal

LA English
AB A cDNA clone coding for a sea urchin embryonic protein was isolated from a prehatching blastula .lambda.gt11 library. The predicted translation product is a secreted 64 .times. 103 Mr enzyme designated as BP10. The protein contains several domains: a ***signal*** ***peptide*** , a putative propeptide, a catalytic domain with an active center typical of a Zn2+-metalloprotease, an EGF-like domain and two internal repeats similar to repeated domains found in the C1s and C1r serine proteases of the complement cascade. The BP10 protease is constructed with the same domains as the human bone morphogenetic protein ***BMP*** -1, a protease described as a factor involved in bone formation, and as the recently characterized product of the tolloid gene which is required for correct dorsal-ventral patterning of the Drosophila embryo. The transcription of the BP10 gene is transiently activated around the 16- to 32-cell stage and the accumulation of BP10 transcripts is limited to a short period at the blastula stage. By in situ hybridization with digoxygeninlabeled RNA probes, the BP10 transcripts were only detected in a limited area of the blastula, showing that the transcription of the BP10 gene is also spatially controlled. Antibodies directed against a fusion protein were used to detect the BP10 protein in embryonic exts. The protein is first detected in early blastula stages, its level peaks in late cleavage, declines abruptly before ingression of primary mesenchyme cells and remains const. in late development. The distribution of the BP10 protein during its synthesis and secretion was analyzed by immunostaining blastula-stage embryos. The intracellular localization of the BP10 staining varies with time. The protein is first detected in a perinuclear region, then in an apical and submembranous position just before its secretion into the perivitelline space. The protein is synthesized in a sharply delimited continuous territory spanning about 70% of the blastula. Comparison of the size and orientation of the labeled territory in the late blastula with the fate map of the blastula stage embryo shows that the domain in which the BP10 gene is expressed corresponds to the presumptive ectoderm. Developing embryos treated with purified antibodies against the BP10 protein and with synthetic peptides derived from the EGF-like domain displayed perturbations in morphogenesis and were radialized to various degrees. These results are consistent with a role for BP10 in the differentiation of ectodermal lineages and subsequent patterning of the embryo. On the basis of these results, the authors speculate that the role of BP10 in the sea urchin embryo might be similar to that of tolloid in Drosophila. They discuss the idea that the processes of spatial regulation of gene expression along the animal-vegetal in sea urchin and dorsal-ventral axes in Drosophila might have some similarities and might use common elements.

L18 ANSWER 51 OF 51 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 11
AN 1990:445943 BIOSIS <<LOGINID::20071018>>
DN PREV199090096583; BA90:96583
TI CLONING AND EXPRESSION OF A WIDELY EXPRESSED RECEPTOR TYROSINE
PHOSPHATASE.
AU SAP J [Reprint author]; D'EUSTACHIO P; GIVOL D; SCHLESSINGER J
CS DEP CHEMICAL IMMUNOLOGY, WEIZMANN INST SCI, REHOVOT 76100, ISRAEL
SO Proceedings of the National Academy of Sciences of the United States of America, (1990) Vol. 87, No. 16, pp. 6112-6116.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 7 Oct 1990
Last Updated on STN: 7 Oct 1990
AB We describe the identification of a widely expressed receptor-type (transmembrane) protein tyrosine phosphatase (PTPase; EC 3.1.3.48). Screening of a mouse brain cDNA library under low-stringency conditions with a probe encompassing the intracellular (phosphatase) domain of the CD45 lymphocyte antigen yielded cDNA clones coding for a 794-amino acid transmembrane protein [hereafter referred to as receptor protein tyrosine phosphatase .alpha. (R-PTP-.alpha.)] with an intracellular domain displaying clear homology to the catalytic domains of CD45 and LAR (45% and 53%, respectively). The 142-amino acid extracellular domain (including ***signal*** ***peptide***) of R-PTP-.alpha. is marked by a high serine/threonine content (32%) as well as eight potential N-glycosylation sites but displays no similarity to known proteins. Genetic mapping assigns the gene for R-PTP-.alpha. to mouse chromosome 2, closely linked to the Il-1a and ***Bmp*** -2a loci. The corresponding mRNA (3.0 kilobases) is expressed in most murine tissues and most abudantly expressed in brain and kidney. Antibodies against a synthetic peptide of R-PTP-.alpha. identified a 130-kDa protein in cells transfected with the R-PTP-.alpha. cDNA.

=> d his

(FILE 'HOME' ENTERED AT 19:29:36 ON 18 OCT 2007)

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 19:32:46 ON 18 OCT 2007
L1 470 S LNP
L2 4688 S LMP
L3 6 S L2 AND HIV TAT
L4 6 DUP REM L3 (0 DUPLICATES REMOVED)
L5 2691 S LMP1
L6 4124 S L5 OR LMP 1
L7 6 S L6 AND PROTEIN TRANSDUCTION DOMAIN
L8 4 S BMP AND PROTEIN TRANSDUCTION DOMAIN
L9 4 DUP REM L8 (0 DUPLICATES REMOVED)
L10 6 S BMP AND HIV TAT
L11 6 DUP REM L10 (0 DUPLICATES REMOVED)
L12 25913 S L2 OR L6 OR BMP
L13 1365 S L12 AND (CHIMER? OR FUSION OR HYBRID OR CONJUGA?)
L14 593 S L13 AND (BONE FORM? OR PROTEOGLYCAN OR DIFFERENT?)
L15 354 DUP REM L14 (239 DUPLICATES REMOVED)
L16 167 S L15 AND PY<=2003
L17 70 S L12 AND (HIV TAT OR VP 22 OR PEP 1 OR ANT OR SIGNAL PEPTIDE)
L18 51 DUP REM L17 (19 DUPLICATES REMOVED)

=> s osteoindu? and protein transduc? domain
L19 4 OSTEOINDU? AND PROTEIN TRANSDUC? DOMAIN

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20 4 DUP REM L19 (0 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L20 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563369 CAPLUS <<LOGINID::20071018>>
DN 147:1976
TI Mechanisms of ***osteoinduction*** by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and BMP agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA Warsaw Orthopedic, Inc., USA; Emory University
SO PCT Int. Appl., 126pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058878	A2	20070524	WO 2006-US43610	20061109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-736191P	P	20051110		

AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptidomimetics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for BMP-2 (bone morphogenetic protein 2) therapeutics. The inventors discovered that LMP-1 can increase cellular responsiveness of mesenchymal stem cells to BMP-2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to BMP-2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L20 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912734 CAPLUS <<LOGINID::20071018>>
DN 147:269173
TI CAMK2 phosphorylation-related mechanism of ***osteoinduction*** by LMP-3 (LIM domain-containing mineralization protein 3), and osteogenic compositions therefor
IN Boden, Scott D.; Sangadala, Sreedhara
PA USA
SO U.S. Pat. Appl. Publ., 17pp., Cont.-in-part of U.S. Ser. No. 385,612.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007191591	A1	20070816	US 2006-633963	20061205
US 2007027081	A1	20070201	US 2006-385612	20060321
PRAI US 2006-772322P	P	20060210		

US 2006-385612 A2 20060321
US 2005-664073P P 20050322
US 2005-664074P P 20050322
US 2005-736191P P 20051110

AB The invention provides novel osteogenic compns. based on Smad ubiquitin regulatory factor-1 (Smurf1)-independent methods of ***osteoinduction*** using LMP-3 (LIM domain-contg. mineralization protein 3). The inventors discovered that a unique amino acid sequence (QNGCRPLTNSRSDRWSQMP) in LMP-3 C-terminus contains a calmodulin kinase 2 (CAMK2) phosphorylation site (QNGCRPLTNSRSDRW). It was also discovered, that LMP-3 competes with Smad1 for phosphorylation by CAMK2. In a broad aspect, the compn. comprises either a first amino acid sequence which is capable of being phosphorylated by CAMK2; or a nucleic acid sequence encoding the first amino acid sequence; or a combination thereof. Optionally, the first amino acid sequence may further comprise a second amino acid sequence which is capable of binding the Smurf1 protein. Further, the compn. may comprise a BMP (bone morphogenetic protein) and/or an agent capable of decreasing an amt. or an activity of CAMK2. The compns. of the instant invention may be incorporated into an implant or delivered via a catheter.

L20 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of ***osteoinduction*** by LMP-1 (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and BMP agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-664073P	P	20050322		
US 2005-664074P	P	20050322		

AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly LMP-1 (LIM mineralization protein-1), to overcome the dose-related translational barriers for BMP-2 (bone morphogenetic protein 2) therapeutics. LMP and BMP agents also include peptide or peptidomimetics-encoding oligonucleotides and LMP and BMP genes. The inventors discovered that LMP-1 can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to BMP-2 and mechanistic elucidation of various aspects of the signaling pathway of LMP-1. It is further demonstrated that LMP-1 interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5. LMP-1 interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in LMP-1, and can be mimicked by a small peptide contg. only that motif. Further, LMP-1 competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to BMP-2. Also LMP-1 is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L20 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of ***osteoinductive*** fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1740600	A1	20070110	EP 2004-749433	20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007505621	T	20070315	JP 2006-526862	20040413
CN 1934123	A	20070321	CN 2004-80008027	20040413
IN 2005KN02097	A	20070810	IN 2005-KN2097	20051024
PRAI US 2003-456551P	P	20030324		
WO 2004-US9127	W	20040413		

AB The invention provides a method for intracellular delivery of ***osteoinductive*** proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an ***osteoinductive*** polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, etc.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l6 and proteoglycan
L21 13 L6 AND PROTEOGLYCAN

=> dup rem l21
PROCESSING COMPLETED FOR L21
L22 10 DUP REM L21 (3 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L22 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:647198 CAPLUS <<LOGINID::20071018>>
DN 147:65618
TI Inducing bone mineralization by expression of the LIM mineralization protein gene to induce aggrecan biosynthesis
IN McKay, William F.; Boden, Scott D.; Yoon, Sangwook T.
PA USA
SO U.S. Pat. Appl. Publ., 91pp., Cont.-in-part of U.S. Ser. No. 382,844.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007134218	A1	20070614	US 2006-602805	20061121
US 2003180266	A1	20030925	US 2002-292951	20021113
US 2003225021	A1	20031204	US 2003-382844	20030307
ZA 2004003714	A	20060222	ZA 2004-3714	20040514
PRAI US 2001-331321P	P	20011114		
US 2002-292951	A2	20021113		
US 2003-382844	A2	20030307		
US 1988-124238	A	19880729		
US 2000-959578	A	20000428		

AB Methods of increasing the levels of a ***proteoglycan*** such as aggrecan in a cell to promote bone mineralization are described. These methods involve increasing the levels of LIM domain-contg. mineralization protein-1 (***LMP*** - ***1***), typically by introduction of an expression cassette for the protein gene. The expression cassette may be delivered as naked DNA, such as a plasmid, or using a viral system. The method can be used to induce ***proteoglycan*** synthesis in osseous cells or to stimulate ***proteoglycan*** or collagen biosynthesis in cells such as intervertebral disk cells including cells of the nucleus pulposus and annulus fibrosus. Antsisense knockdown of ***LMP*** - ***1*** gene expression in osteoblasts prevented mineral nodule formation and osteocalcin secretion. CDNAs for LIM proteins functional in membranous bone formation (designated ***LMP*** - ***1***) were cloned and sequenced from rat osteoblasts and human cDNA libraries. Human LMP has several splicing isoforms and the gene encoding human ***LMP*** - ***1*** was sequenced. Methods of expressing the LIM mineralization protein gene and assessing glycosylation of the LIM mineralization protein in prokaryotic and non-mammalian eukaryotic cells are also described. Transfection with an adenoviral vector expressing human ***LMP*** - ***1*** is effective in increasing ***proteoglycan*** synthesis of intervertebral disk cells. The dose of virus leading to the highest transgene expression (MOI 1000) also leads to the highest induction of sol. glycosaminoglycans, suggesting a correlation between ***LMP*** - ***1*** levels and sol. glycosaminoglycan biosynthesis. These data indicate that hLMP-1 gene therapy is a method of increasing ***proteoglycan*** synthesis in the intervertebral disk, and that hLMP-1 is an agent for treating disk disease.

L22 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:486422 CAPLUS <<LOGINID::20071018>>

DN 146:476694
TI Expression of LIM mineralization protein in mammalian cells for gene therapy of bone formation
IN Boden, Scott D.; Sangadala, Sreedhara; Titus, F. Louisa; McKay, William F.
PA USA
SO U.S. Pat. Appl. Publ., 70pp., Cont.-in-part of U.S. Ser. No. 292,951.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007099176	A1	20070503	US 2006-545349	20061010
US 2003180266	A1	20030925	US 2002-292951	20021113
CN 1665391	A	20050907	CN 2002-827099	20021114
ZA 2004003714	A	20060222	ZA 2004-3714	20040514
PRAI US 2001-331321P	P	20011114		
US 2002-292951	A2	20021113		
US 1988-124238	A	19880729		
US 2000-959578	A	20000428		

AB LIM domain-contg. proteins involved in bone formation and methods of expressing LIM mineralization protein in mammalian cells are described. LIM proteins functional in membraneous bone formation (designated ***LMP*** - ***1***) are cloned and sequenced from rat osteoblasts and human cDNA libraries; human LMP exists as several spliced isoforms and the genomic sequence encoding human ***LMP*** - ***1*** was detd. Methods of expressing LIM mineralization protein and assessing glycosylation of the LIM mineralization protein in prokaryotic and non-mammalian eukaryotic cells are also described. The methods involve transfecting the cells with an isolated nucleic acid comprising a nucleotide sequence encoding a LIM mineralization protein (LMP). Transfection may be accomplished in vitro, ex vivo or in vivo by direct injection of virus or naked DNA, or by a nonviral vector such as a plasmid. Transfection with an adenoviral vector expressing human ***LMP*** - ***1*** is effective in increasing ***proteoglycan*** synthesis of intervertebral disk cells. The dose of virus leading to the highest transgene expression (MOI 1000) also leads to the highest induction of sol. glycosaminoglycans, suggesting a correlation between hLMP-1 expression and sol. glycosaminoglycan induction. These data indicate that hLMP-1 gene therapy is a method of increasing ***proteoglycan*** synthesis in the intervertebral disk, and that hLMP-1 is an agent for treating disk disease.

L22 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1740600	A1	20070110	EP 2004-749433	20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007505621	T	20070315	JP 2006-526862	20040413
CN 1934123	A	20070321	CN 2004-80008027	20040413
IN 2005KN02097	A	20070810	IN 2005-KN2097	20051024
PRAI US 2003-456551P	P	20030324		
WO 2004-US9127	W	20040413		

AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote ***proteoglycan*** synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, etc.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:638797 CAPLUS <<LOGINID::20071018>>
DN 145:468741
TI LIM mineralization protein-1 in spinal surgery
AU Bai, Yushu; Hou, Tiesheng
CS Changhai Hospital, Second Military Medical University of Chinese PLA, Shanghai, 200433, Peop. Rep. China
SO Zhongguo Linchuang Kangfu (2005), 9(30), 175-177
CODEN: ZLKHAH; ISSN: 1671-5926
PB Zhongguo Linchuang Kangfu Zazhishe
DT Journal; General Review
LA Chinese
AB A review. LIM mineralization protein-1 is a non-secreted intracellular protein, which induces ossification directly and indirectly, mediates the metab. of bone morphogenetic protein, ***proteoglycan*** , and collagen. The advancing and developing status of the protein in exptl. study of spinal surgery are summarized. LIM mineralization protein-1 is an effective osteoblast promoter, and its modification and control are realized through bone morphogenetic protein. LIM mineralization protein-1 effect on intervertebral disk and vertebral body degenerative modification are complex, and further study is needed.

L22 ANSWER 5 OF 10 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2005539646 EMBASE <<LOGINID::20071018>>
TI Molecular therapy of the intervertebral disc.
AU Yoon S.T.
CS Dr. S.T. Yoon, Emory Spine Center, 59 Executive Park South, Atlanta, GA 30029, United States. tim_yoon@emoryhealthcare.org
SO Spine Journal, (Nov 2005) Vol. 5, No. 6 SUPPL., pp. 280S-286S.
Refs: 45
ISSN: 1529-9430 CODEN: SJPOA6
PUI S 1529-9430(05)00095-1
CY United States
DT Journal; General Review; (Review)
FS 022 Human Genetics
030 Clinical and Experimental Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
039 Pharmacy
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 15 Dec 2005
Last Updated on STN: 15 Dec 2005
AB Background and context: Currently, no biologic treatment is available for disc degeneration. However, many different molecules of potential therapeutic benefit are being investigated. Purpose: Review and categorize the molecules under investigation for potential therapy in preventing or reversing disc degeneration. Study design: Review article. Methods: Review of published articles on molecules that may be useful in biologic therapy of the intervertebral disc. Results: The list of molecules under investigation for potential benefit in biologic therapy of the intervertebral disc repair continues to grow. These molecules are so diverse that they no longer all fall into the classic terminology of "growth factor." Some of these molecules are not growth factors at all and some are not even cytokines. At least four different classes of molecules may be effective in disc repair. These include anticatabolics (eg, tissue inhibitors of metalloproteinase [TIMPs]), mitogens (eg, insulin-like growth factor-1 [IGF-1], platelet-derived growth factor [PDGF]), chondrogenic morphogens (transforming growth factor .beta. [TGF-.beta.] and bone morphogenetic proteins [BMPs]), and intracellular regulators (LIM mineralization protein-1 [***LMP*** - ***1***] and Sox9). Although some in vitro data are available on all of these molecules, few of these molecules have been tested in vivo with an animal model of disc degeneration. Conclusions: As the current screening experiments are concluded, more definitive in vivo systems involving a more realistic degeneration model will be a necessary step before attempting human studies. .COPYRGT. 2005 Elsevier Inc. All rights reserved.

L22 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2005:99845 BIOSIS <<LOGINID::20071018>>
DN PREV200500097544
TI ISSLS prize winner: ***LMP*** - ***1*** upregulates intervertebral disc cell production of proteoglycans and BMPs in vitro and in vivo.
AU Yoon, Sangwook Tim [Reprint Author]; Park, Jin Soo; Kim, Keun S.; Li, Jun; Attallah-Wasif, Emad Samir; Hutton, William C.; Boden, Scott D.
CS Sch MedEmory Spine CtrDept Orthopaed Surg, Emory Univ, 2165 N Decatur Rd,
Decatur, GA, 30033, USA
tim_yoon@emoryhealthcare.org
SO Spine, (December 1 2004) Vol. 29, No. 23, pp. 2603-2611. print.
ISSN: 0362-2436 (ISSN print).
DT Article
LA English
ED Entered STN: 9 Mar 2005
Last Updated on STN: 9 Mar 2005
AB Study Design. Experiments using both in vitro tissue culture and in vivo rabbit methods were used to study the effect of Lim Mineralization Protein-1 (***LMP*** - ***1***) on intervertebral disc (IVD) cell production of proteoglycans and bone morphogenetic proteins (BMPs). Objectives. To determine the effect of ***LMP*** - ***1*** overexpression in IVD cells on the production of proteoglycans and BMPs

both in vitro and in vivo and to show that ***LMP*** - ***1*** mediates the control of ***proteoglycan*** production through its action on BMPs. Summary of Background Data. Because BMPs are known to increase ***proteoglycan*** synthesis and ***LMP*** - ***1*** is known to upregulate BMPs in certain cells, it was hypothesized that ***LMP*** - ***1*** may increase ***proteoglycan*** production in IVD cells. Methods. DMMB, real-time polymerase chain reaction, and ELISA methods were used to quantitate ***proteoglycan*** , mRNA, and protein levels, respectively. Noggin was used to block the effect of the adenovirus carrying ***LMP*** - ***1*** (AdLMP-1) on ***proteoglycan*** synthesis. In vivo experiments using intradiscal AdLMP-1 injection were performed with New Zealand White rabbits. Three weeks later, the mRNA levels of ***LMP*** - ***1*** , aggrecan, BMP-2, and BMP-7 were measured. Results. In vitro experiments revealed that the sulfated glycosaminoglycan (sGAG) and aggrecan mRNA levels were significantly increased with AdLMP-1 treatment. Similarly, BMP-2 and BMP-7 mRNA and protein levels increased significantly, but BMP-4 and BMP-6 levels were unchanged. Noggin blocked the upregulation of ***proteoglycan*** by AdLMP-1. In vivo discs injected with AdLMP-1 had significantly elevated levels of ***LMP*** - ***1*** , BMP-2, and BMP-7 mRNA. Conclusions. ***LMP*** - ***1*** overexpression increases disc cellproduction of ***proteoglycan*** , BMP-2, and BMP-7. LMP-1mediates the control of ***proteoglycan*** production through its action on BMP.

L22 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:764373 CAPLUS <<LOGINID::20071018>>
DN 141:328901
TI BMP and ***LMP*** - ***1*** for intervertebral disc regeneration
AU Park, Jin Soo; Nagata, Kensei
CS Department of Orthopaedic Surgery, Kurume University School of Medicine, Japan
SO Clinical Calcium (2004), 14(7), 1096-1098
CODEN: CLCCEJ; ISSN: 0917-5857
PB Iyaku Janarusha
DT Journal; General Review
LA Japanese
AB A review. Some evidence indicates that intervertebral disk degeneration is assocd. with decreasing of matrix synthesis from disk cell. BMP-2 increased mRNA of aggrecan and type II collagen. It also enhanced disk matrix (***proteoglycan***) prodn. Adenovirally mediated ***LMP*** - ***1*** overexpression in intervertebral disk cells increased disk cell ***proteoglycan*** prodn. through a process medicated by BMP-2 and BMP-7.

L22 ANSWER 8 OF 10 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004055342 EMBASE <<LOGINID::20071018>>
TI The potential of gene therapy for the treatment of disc degeneration.
AU Yoon S.T.
CS Dr. S.T. Yoon, Department of Orthopaedics, Emory University, Emory Orthopaedics and Spine Center, 59 Executive Park South, Atlanta, GA 30033, United States. tim_yoon@emoryhealthcare.org
SO Orthopedic Clinics of North America, (Jan 2004) Vol. 35, No. 1, pp. 95-100.
Refs: 45
ISSN: 0030-5898 CODEN: OCLNAQ
CY United States
DT Journal; General Review; (Review)
FS 022 Human Genetics
030 Clinical and Experimental Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
039 Pharmacy
LA English
SL English
ED Entered STN: 26 Feb 2004
Last Updated on STN: 26 Feb 2004
AB Research in biologic methods of treating disc degeneration is still in its infancy. Many different strategies are being evaluated, but the gene therapy strategy stands out because of its potential for longterm efficacy. Choosing the correct gene for use in gene therapy is critically important. Of the many different classes of potentially therapeutic genes, the regulatory genes hold the most promise. Of the different gene therapy delivery methods, the most work has been performed with viral vectors, either ex vivo or in vivo. Current research now is turning toward in vivo experiments in rabbits. Efficacy and safety will be demonstrated first with smaller animal models. Beyond that, nonhuman primate experiments demonstrating efficacy and safety will be the penultimate step before initiation of human studies.

L22 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:950040 CAPLUS <<LOGINID::20071018>>
DN 140:19764
TI Methods of inducing the expression of bone morphogenetic proteins (BMPs) and transforming growth factor-beta proteins (TGF-.beta.s) in cells
IN Mckay, William F.; Boden, Scott D.; Yoon, Sangwook T.
PA Medtronic Sofamor Danek, USA
SO U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S. Ser. No. 292,951.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003225021	A1	20031204	US 2003-382844	20030307
US 2003180266	A1	20030925	US 2002-292951	20021113
CN 1665391	A	20050907	CN 2002-827099	20021114
AU 2004271093	A1	20050317	AU 2004-271093	20040307
CA 2518295	A1	20050317	CA 2004-2518295	20040307
WO 2005023996	A2	20050317	WO 2004-US7616	20040307
WO 2005023996	A3	20051229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1629106	A2	20060301	EP 2004-749373	20040307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1777680	A	20060524	CN 2004-80010171	20040307
JP 2006519622	T	20060831	JP 2006-509245	20040307
ZA 2004003714	A	20060222	ZA 2004-3714	20040514
IN 2005KN01988	A	20061208	IN 2005-KN1988	20051006
US 2007134218	A1	20070614	US 2006-602805	20061121
PRAI US 2001-331321P	P	20011114		
US 2002-292951	A2	20021113		
US 1988-124238	A	19880729		
US 2000-959578	A	20000428		
US 2003-382844	A	20030307		
WO 2004-US7616	W	20040307		

AB A method of inducing the expression of one or more bone morphogenetic proteins and/or transforming growth factor-.beta. proteins in a cell is described. The method includes transfecting a cell with an isolated nucleic acid comprising a nucleotide sequence encoding a LIM mineralization protein operably linked to a promoter. The one or more bone morphogenetic proteins can be BMP-2, BMP-4, BMP-6, BMP-7 or combinations thereof. The transforming growth factor-.beta. protein can be transforming growth factor-.beta.1 protein (TGF-.beta.1). Transfection may be accomplished ex vivo or in vivo by direct injection of virus or naked DNA, or by a nonviral vector such as a plasmid. The method can be used to induce bone formation in osseous cells or to stimulate ***proteoglycan*** and/or collagen prodn. in cells capable of producing proteoglycyan and/or collagen (e.g., intervertebral disk cells).

L22 ANSWER 10 OF 10 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2
AN 1999:213731 BIOSIS <<LOGINID::20071018>>
DN PREV199900213731
TI Human immunodeficiency virus-associated Hodgkin's disease derives from post-germinal center B cells.
AU Carbone, Antonino [Reprint author]; Gloghini, Annuziata; Larocca, Luigi M.; Antinori, Andrea; Falini, Brunangelo; Tirelli, Umberto; Dalla-Favera, Riccardo; Gaidano, Gianluca
CS Division of Pathology, Centro di Riferimento Oncologico, Istituto Nazionale Tumori, IRCCS, via Pedemontana Occidentale, Aviano, I-33081, Italy
SO Blood, (April 1, 1999) Vol. 93, No. 7, pp. 2319-2326. print.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Article
LA English
ED Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999
AB Human immunodeficiency virus-associated Hodgkin's disease (HIV-HD) displays several peculiarities when compared with HD of the general population. These include overrepresentation of clinically aggressive histologic types and frequent infection of Reed-Sternberg (RS) cells by Epstein-Barr virus (EBV). Recently, we have reported that the histogenesis of HD of the general population may be assessed by monitoring the expression pattern of BCL-6, a transcription factor expressed in germinal center (GC) B cells, and of CD138/syndecan-1 (syn-1), a ***proteoglycan*** associated with post-GC, terminal B-cell differentiation. In this study, we have applied these two markers to the study of HIV-HD histogenesis and correlated their expression status to the virologic features of this disease. We have found that RS cells of all histologic categories of HIV-HD consistently display the BCL-6-/syn-1+ phenotype and thus reflect post-GC B cells. Although BCL-6-/syn-1+ RS cells of HIV-HD express CD40, they are not surrounded by CD40 ligand-positive (CD40L+) reactive T lymphocytes, which, in HD of the general population, are thought to regulate the disease phenotype through CD40/CD40L interactions. Conversely, RS cells of virtually all HIV-HD express the EBV-encoded latent membrane protein 1 (***LMP1***), which, being functionally homologous to CD40, may contribute, at least in part, to the modulation of the HIV-HD phenotype.

=> s l6 and (sulfated glycosaminoglycan or sGAG)
L23 2 L6 AND (SULFATED GLYCOSAMINOGLYCAN OR SGAG)

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24 1 DUP REM L23 (1 DUPLICATE REMOVED)

=> d bib abs

L24 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2005:99845 BIOSIS <<LOGINID::20071018>>
DN PREV200500097544
TI ISSLS prize winner: ***LMP*** - ***1*** upregulates intervertebral disc cell production of proteoglycans and BMPs in vitro and in vivo.
AU Yoon, Sangwook Tim [Reprint Author]; Park, Jin Soo; Kim, Keun S.; Li, Jun; Attallah-Wasif, Emad Samir; Hutton, William C.; Boden, Scott D.
CS Sch MedEmory Spine CtrDept Orthopaed Surg, Emory Univ, 2165 N Decatur Rd,
Decatur, GA, 30033, USA
tim_yoon@emoryhealthcare.org
SO Spine, (December 1 2004) Vol. 29, No. 23, pp. 2603-2611. print.
ISSN: 0362-2436 (ISSN print).
DT Article
LA English
ED Entered STN: 9 Mar 2005
Last Updated on STN: 9 Mar 2005
AB Study Design. Experiments using both in vitro tissue culture and in vivo rabbit methods were used to study the effect of Lim Mineralization Protein-1 (***LMP*** - ***1***) on intervertebral disc (IVD) cell production of proteoglycans and bone morphogenetic proteins (BMPs). Objectives. To determine the effect of ***LMP*** - ***1*** overexpression in IVD cells on the production of proteoglycans and BMPs both in vitro and in vivo and to show that ***LMP*** - ***1*** mediates the control of proteoglycan production through its action on BMPs. Summary of Background Data. Because BMPs are known to increase proteoglycan synthesis and ***LMP*** - ***1*** is known to upregulate BMPs in certain cells, it was hypothesized that ***LMP*** - ***1*** may increase proteoglycan production in IVD cells. Methods. DMMB, real-time polymerase chain reaction, and ELISA methods were used to quantitate proteoglycan, mRNA, and protein levels, respectively. Noggin was used to block the effect of the adenovirus carrying ***LMP*** - ***1*** (AdLMP-1) on proteoglycan synthesis. In vivo experiments using intradiscal AdLMP-1 injection were performed with New Zealand White rabbits. Three weeks later, the mRNA levels of ***LMP*** - ***1*** , aggrecan, BMP-2, and BMP-7 were measured. Results. In vitro experiments revealed that the ***sulfated*** ***glycosaminoglycan*** (***sGAG***) and aggrecan mRNA levels were significantly increased with AdLMP-1 treatment. Similarly, BMP-2 and BMP-7 mRNA and protein levels increased significantly, but BMP-4 and BMP-6 levels were unchanged. Noggin blocked the upregulation of proteoglycan by AdLMP-1. In vivo discs injected with AdLMP-1 had significantly elevated levels of ***LMP*** - ***1*** , BMP-2, and BMP-7 mRNA. Conclusions. ***LMP*** - ***1*** overexpression increases disc cellproduction of proteoglycan, BMP-2, and BMP-7. LMP-1mediates the control of proteoglycan production through its action on BMP.

=> s osteoblast (3a) differentiat?
L25 7949 OSTEOBLAST (3A) DIFFERENTIAT?

=> s l25 and l6
L26 26 L25 AND L6

=> dup rem l26
PROCESSING COMPLETED FOR L26
L27 16 DUP REM L26 (10 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

L27 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563369 CAPLUS <<LOGINID::20071018>>
DN 147:1976
TI Mechanisms of osteoinduction by ***LMP*** - ***1*** (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and BMP agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.; Sangadala, Sreedhara
PA Warsaw Orthopedic, Inc., USA; Emory University
SO PCT Int. Appl., 126pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058878	A2	20070524	WO 2006-US43610	20061109

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-736191P P 20051110
AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptidomimetics of LIM domain-contg. mineralization proteins (LMPs), particularly ***LMP*** - ***1*** (LIM mineralization protein-1), to overcome the dose-related translational barriers for BMP-2 (bone morphogenetic protein 2) therapeutics. The inventors discovered that ***LMP*** - ***1*** can increase cellular responsiveness of mesenchymal stem cells to BMP-2 and mechanistic elucidation of various aspects of the signaling pathway of ***LMP*** - ***1*** . It is further demonstrated that ***LMP*** - ***1*** interacts in vitro an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5. ***LMP*** - ***1*** interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in ***LMP*** - ***1*** , and can be mimicked by a small peptide contg. only that motif. Further, ***LMP*** - ***1*** competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to BMP-2. Also ***LMP*** - ***1*** is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L27 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2007:506360 BIOSIS <<LOGINID::20071018>>
DN PREV200700501701
TI Semi-quantitative RT-PCR analysis of LIM mineralization protein 1 and its associated molecules in cultured human dental pulp cells.
AU Zhang, Qi; Wang, Xiaoying; Chen, Zhuo; Liu, Gang; Chen, Zhi [Reprint Author]
CS Wuhan Univ, Sch and Hosp Stromatol, Minist Educ, Key Lab Oral Biomed Engn,
Luoyu Rd 237, Wuhan 460079, Hubei Province, Peoples R China
zhichen@whu.edu.cn
SO Archives of Oral Biology, (AUG 2007) Vol. 52, No. 8, pp. 720-726.
CODEN: AOBIAR. ISSN: 0003-9969.
DT Article
LA English
ED Entered STN: 26 Sep 2007
Last Updated on STN: 26 Sep 2007
AB Objective: LIM mineralization protein 1 (***LMP*** - ***1***), an intracellular signaling molecule, regulates ***osteoblast*** ***differentiation*** and maturation, as well as bone formation. However, the role of ***LMP*** - ***1*** in the differentiation of human dental pulp cells and formation of dentin has not been determined. The study was to investigate the expression of ***LMP*** - ***1*** , the related proteins, such as bone morphogenetic proteins 2, 6 and 7 (BMP-2, BMP-6 and BMP-7), and core binding factor alpha 1 (Cbfa1) during the differentiation of cultured human dental pulp cells and the formation of mineralized nodules.Design: Differentiation of human dental pulp cells was induced by dexamethasone, asorbic acid and p-glycerophosphate. The formation of mineralized nodules, was determined by Von Kossa staining and immunocytochemistry detection of dentin sialoprotein. Expression of ***LMP*** - ***1*** , the related proteins and the differentiation marker alkaline phosphatase (ALP) was anatysed by reverse transcriptase-polymerase chain reaction (RT-PCR).Results: The expression of ***LMP*** - ***1*** , BMP-2, BMP-6, BMP-7 and Cbfa1 was significantly increased in the process of dental pulp cells differentiation and the formation of mineralized nodules, while the pattern of the expression was distinct. Conclusions: The elevated level of ***LMP*** - ***1*** , BMPs and Cbfa1 expression indicated they might play a role in the differentiation of human dental pulp cells and the formation of mineralized nodules. (C) 2007 Elsevier Ltd. All rights reserved.

L27 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1011760 CAPLUS <<LOGINID::20071018>>
DN 145:369831
TI Mechanisms of osteoinduction by ***LMP*** - ***1*** (LIM mineralization protein-1), and a method of a co-therapeutic treatment of bone conditions by LMP and BMP agents
IN Marx, Jeffrey C.; McKay, William F.; Boden, Scott D.
PA Sdgi Holdings, Inc., USA
SO PCT Int. Appl., 64pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006102417	A2	20060928	WO 2006-US10419	20060322

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-664073P P 20050322
US 2005-664074P P 20050322

AB The present invention relates to the methods and compns. for the treatment of subjects having compromised bone conditions. Specifically, the invention relates to combinatorial therapeutic strategies including small mols. and peptide mimics of LIM domain-contg. mineralization proteins (LMPs), particularly ***LMP*** - ***1*** (LIM mineralization protein-1), to overcome the dose-related translational barriers for BMP-2 (bone morphogenetic protein 2) therapeutics. LMP and BMP agents also include peptide or peptidomimetics-encoding oligonucleotides and LMP and BMP genes. The inventors discovered that ***LMP*** - ***1*** can dramatically increase cellular responsiveness of mesenchymal stem cells (MSCs) to BMP-2 and mechanistic elucidation of various aspects of the signaling pathway of ***LMP*** - ***1*** . It is further demonstrated that ***LMP*** - ***1*** interacts in vitro and co-immunoppt. with an 85 kDa protein, identified as Smurf1, a regulator of the degrdn. of BMP-2 signaling mols., Smad1 and Smad5. ***LMP*** - ***1*** interaction occurs with the Smurf WW2 domain, and is dependent on a specific PY motif in ***LMP*** - ***1*** , and can be mimicked by a small peptide contg. only that motif. Further, ***LMP*** - ***1*** competitively binds to Smurf1, preventing ubiquitin-mediated proteasomal degrdn. of Smads, contributing to an enhanced cellular responsiveness to BMP-2. Also ***LMP*** - ***1*** is shown to interact with Jab1, an adaptor protein which regulates degrdn. of the Smad4 resulting in increased nuclear Smad4.

L27 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:932971 CAPLUS <<LOGINID::20071018>>
DN 146:55863
TI Is 1, 25-dihydroxyvitamin D3 an ideal substitute for dexamethasone for inducing osteogenic differentiation of human adipose tissue-derived stromal cells in vitro?
AU Zhou, Yong-sheng; Liu, Yun-song; Tan, Jian-guo
CS Department of Prosthodontics, School and Hospital of Stomatology, Peking University, Beijing, 100081, Peop. Rep. China
SO Chinese Medical Journal (Beijing, China, English Edition) (2006), 119(15), 1278-1286
CODEN: CMJODS; ISSN: 0366-6999
PB Chinese Medical Association
DT Journal
LA English
AB Background: Human adipose tissue-derived stromal cells (hADSCs) can be induced to differentiate along an osteoblastic lineage under stimulation of dexamethasone (DEX). Recent studies, however, have questioned the efficacy of glucocorticoids such as DEX in mediating the osteogenesis process of skeletal progenitor cells and processed lipoaspirate cells. Is it possible to find a substitute for DEX. Therefore, this study was designed to investigate osteogenic capacity and regulating mechanisms for osteoblastic differentiation of hADSCs by comparing osteogenic media (OM) contg. either 1, 25-dihydroxyvitamin D3 (VD) or DEX and det. if VD was an ideal substitute for DEX as an induction agent for the osteogenesis of hADSCs. Methods: Osteogenic differentiation of hADSCs was induced by osteogenic medium (OM) contg. either 10 nmol/L VD or 100 nmol/L DEX. Differentiation of hADSCs into osteoblastic lineage was identified by alk. phosphatase (ALP) staining, von Kossa staining, and reverse transcription-polymerase chain reaction assays for mRNA expression of osteogenesis-related genes such as type I collagen (COL I), bone sialoprotein (BSP), osteocalcin (OC), bone morphogenetic protein (BMP)-2, BMP-4, BMP-6, BMP-7, runt-related transcription factor 2/core binding factor .alpha.1 (Runx2/Cbfa1), osterix (Osx), and LIM mineralization protein-1 (***LMP*** - ***1***). Results: von Kossa staining revealed that the differentiated cells induced by both VD and DEX were mineralized in vitro. They also expressed osteoblast-related markers, such as ALP, COL I, BSP, and OC. Runx2/Cbfa1, Osx, BMP-6, and ***LMP*** - ***1*** were upregulated during VD and DEX-induced hADSC osteoblastic differentiation, but BMP-4, BMP-7 were not. BMP-2 was only expressed in VD-induced differentiated cells. Conclusions: VD or DEX-induced hADSCs differentiate toward the osteoblastic lineage in vitro. Runx2/Cbfa1, Osx, BMP-2, BMP-6, and ***LMP*** - ***1*** are involved in regulating osteoblastic differentiation of hADSCs, but BMP-4, BMP-7 are not. VD, but not DEX, induces expression of BMP-2 during osteogenic induction of hADSCs. VD is an ideal substitute for DEX for osteogenic induction of hADSCs.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1239076 CAPLUS <<LOGINID::20071018>>
DN 144:641
TI Intracellular delivery of osteoinductive fusion proteins for inducing bone formation and disc regeneration
IN Titus, Frances; Marx, Jeffrey; Drapeau, Susan; Boden, Scott; Yoon, Sangwook
PA Medtronic Sofamor Danek, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005111058	A1	20051124	WO 2004-US9127	20040413
WO 2005111058	A9	20070118		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1740600	A1	20070110	EP 2004-749433	20040413
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007505621	T	20070315	JP 2006-526862	20040413
CN 1934123	A	20070321	CN 2004-80008027	20040413
IN 2005KN02097	A	20070810	IN 2005-KN2097	20051024

PRAI US 2003-456551P P 20030324
WO 2004-US9127 W 20040413

AB The invention provides a method for intracellular delivery of osteoinductive proteins fused with transduction domains and uses of the fusion proteins to induce osteogenesis and to promote proteoglycan synthesis. An expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide is introducing into suitable host cells such as multipotent progenitor cells to induce bone formation in vivo. The cell-permeable polypeptide may be chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, etc.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2005:531652 BIOSIS <<LOGINID::20071018>>
DN PREV200510325167
TI Insulin-like growth factor binding protein (BP)-6 inhibits ***osteoblast*** ***differentiation*** and binds to LIM mineralization protein-1 (***LMP*** - ***1***), an intracellular protein that stimulates ***osteoblast*** ***differentiation*** .
AU Strong, Donna Dee [Reprint Author]; Amaar, Yousef; Mohan, Subburaman; Linkhart, Thomas A
CS VA Loma Linda Healthcare Syst, Loma Linda, CA 92357 USA
SO FASEB Journal, (MAR 4 2005) Vol. 19, No. 4, Suppl. S, Part 1, pp. A742. Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci. CODEN: FAJOEC. ISSN: 0892-6638.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005
AB We found that BP-6 strongly inhibited ***osteoblast*** ***differentiation*** by an IGF-independent mechanism. Because BP-6 is in the nucleus, we tested whether BP-6 could inhibit differentiation by binding to and sequestering transcription factors that regulate osteoblast gene expression. To identify interacting proteins, BP-6 fused to the Gal-4 DNA binding domain was used as bait in a yeast two-hybrid screen of a U-2 OS osteosarcoma library. BP-6 interacted strongly with ***LMP*** - ***1*** , a member of a diverse family of LIM domain proteins, that stimulates ***osteoblast*** ***differentiation*** in vitro and induces bone formation in vivo when expressed from an adenoviral vector in a spinal fusion model (Viggeswarapu, et al. 2001). We found that ***LMP*** - ***1*** stimulated transcription of the type I procollagen promoter by a BMP independent mechanism when coexpressed in osteoblasts. Coimmunoprecipitation studies revealed that intact ***LMP*** - ***1*** protein interacted with BP-6but not IGFBP-5 when ***LMP*** - ***1*** was coexpressed in cells, demonstrating specificity. When BP-6 and ***LMP*** - ***1*** -fluorescent fusion proteins were transiently co-expressed in osteoblasts, ***LMP*** - ***1*** and BP-6 colocalized in the nucleus. The findings that ***LMP*** - ***1*** strongly binds to BP-6, an inhibitor of ***osteoblast*** ***differentiation*** andthat ***LMP*** - ***1*** is a positive regulator of ***osteoblast*** ***differentiation*** is consistent with the hypothesis that BP-6 sequesters ***LMP*** - ***1*** to inhibit differentiation.

L27 ANSWER 7 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2006:195629 BIOSIS <<LOGINID::20071018>>
DN PREV200600200317
TI Increasing BMP responsiveness in human mesenchymal stem cells in vitro by addition of the osteoinductive ***LMP*** - ***1*** gene.
AU Viggeswarapu, M. [Reprint Author]; Bargouti, M.; Teklemariam, M.; Baker, N.; Rogers, C.; Zhu, L.; Titus, L.; Boden, S. D.

CS Emory Univ, Decatur, GA USA
SO Journal of Bone and Mineral Research, (SEP 2005) Vol. 20, No. 9, Suppl. 1, pp. S359.
Meeting Info.: 27th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research. Nashville, TN, USA. September 23 -27, 2005. Amer Soc Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 22 Mar 2006
Last Updated on STN: 22 Mar 2006

L27 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2006:194668 BIOSIS <<LOGINID::20071018>>
DN PREV200600199356
TI Non-canonical Wnt 11 transcriptionally suppresses expression of insulin-like growth factor binding protein-6, an inhibitor of ***osteoblast*** ***differentiation*** .
AU Strohbach, C. [Reprint Author]; Linkhart, T. A.; Mohan, S.; Shi, Y.; Glackin, C.; Strong, D. D.
CS VA Loma Linda Healthcare Syst, Res 151, Loma Linda, CA USA
SO Journal of Bone and Mineral Research, (SEP 2005) Vol. 20, No. 9, Suppl. 1, pp. S129-S130.
Meeting Info.: 27th Annual Meeting of the American-Society-for-Bone-and-Mineral-Research. Nashville, TN, USA. September 23 -27, 2005. Amer Soc Bone & Mineral Res.
CODEN: JBMREJ. ISSN: 0884-0431.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 22 Mar 2006
Last Updated on STN: 22 Mar 2006

L27 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:825023 CAPLUS <<LOGINID::20071018>>
DN 141:325787
TI Intracellular delivery expression construct encoding fusion protein of osteoinductive proteins and peptides and use to induce bone formation
IN Titus, Frances Louisa; Marx, Jeffrey C.; Boden, Scott D.; Yoon, Sangwook T.; Drapeau, Susan
PA USA
SO U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004197867	A1	20041007	US 2004-806915	20040323
CA 2517496	A1	20040924	CA 2004-2517496	20040324
AU 2004317501	A1	20051124	AU 2004-317501	20040324
PRAI US 2003-456551P	P	20030324		

AB The present invention provides a method of producing a cell-permeable osteoinductive polypeptide comprising introducing into a suitable host cell an expression construct encoding a cell-permeable polypeptide and an osteoinductive polypeptide positioned so that the osteoinductive polypeptide is expressed as part of a fusion protein with the cell-permeable polypeptide. The invention also provides osteoinductive peptides which have demonstrated the ability to induce bone formation in vivo. The invention further relates to that the cell-permeable polypeptide may be chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, etc.

L27 ANSWER 10 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 2
AN 2004:269666 BIOSIS <<LOGINID::20071018>>
DN PREV200400264789
TI Efficient bone formation by gene transfer of human LIM mineralization protein-3.
AU Pola, E; Gao, W; Zhou, Y; Pola, R; Lattanzi, W; Sfeir, C; Gambotto, A; Robbins, PD [Reprint Author]
CS Med CtrDept Mol Genet & Biochem, Univ Pittsburgh, W1246 Biomed Sci Tower,
Pittsburgh, PA, 15261, USA
SO Gene Therapy, (April 2004) Vol. 11, No. 8, pp. 683-693. print.
ISSN: 0969-7128 (ISSN print).
DT Article
LA English
ED Entered STN: 26 May 2004
Last Updated on STN: 26 May 2004
AB LIM mineralization protein (LMP) is a novel positive regulator of the ***osteoblast*** ***differentiation*** program. In humans, three different LMP splice variants have been identified: ***LMP*** - ***1*** , LMP-2, and LMP-3. Gene transfer of human ***LMP*** - ***1*** (hLMP-1) induces expression of genes involved in bone formation, including certain bone morphogenetic proteins (BMPs), promotes bone nodule formation in vitro, ectopic bone formation in vivo, and is therapeutic in animal models of posterior thoracic and lumbar spine fusion. To examine the osteoinductive properties of the LMP-3 in vitro and in vivo, we have generated plasmid and adenoviral vectors expressing codon-optimized hLMP-3. Here we demonstrate that gene transfer of hLMP-3 induces expression of the bone-specific genes osteocalcin, osteopontin, and bone sialoprotein and induced bone mineralization in preosteoblastic and fibroblastic cells. We also demonstrate that hLMP-3 is able to induce bone mineralization and the expression of the bone-specific genes, BMP-2, OSX, RunX2, and alkaline phosphatase in human mesenchymal stem cells in a dose-dependent manner. Finally, we demonstrate that direct gene transfer of hLMP-3 into murine skeletal muscle results in ectopic bone formation more efficiently than BMP-2. These results demonstrate that hLMP-3 gene transfer can be used to promote bone formation in cell culture and in vivo as or more efficiently than BMP-2, thus establishing feasibility and efficacy of direct gene delivery of hLMP-3 to produce bone in vivo. These results suggest that gene transfer of hLMP-3 could be developed as a bone-inductive therapeutic agent for clinical applications.

L27 ANSWER 11 OF 16 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2003221377 EMBASE <<LOGINID::20071018>>
TI Mechanism of bone formation with gene transfer of the cDNA encoding for the intracellular protein ***LMP*** - ***1*** .
AU Minamide A.; Boden S.D.; Viggeswarapu M.; Hair G.A.; Oliver C.; Titus L.
CS Dr. A. Minamide, Department of Orthopaedic Surgery, Emory Spine Center, Emory University School of Medicine, 2165 North Decatur Road, Decatur, GA 30033, United States. scott_boden@emoryhealthcare.org
SO Journal of Bone and Joint Surgery - Series A, (1 Jun 2003) Vol. 85, No. 6, pp. 1030-1039.
Refs: 19
ISSN: 0021-9355 CODEN: JBJSA3
CY United States
DT Journal; Article
FS 022 Human Genetics
033 Orthopedic Surgery
037 Drug Literature Index
LA English
SL English
ED Entered STN: 19 Jun 2003
Last Updated on STN: 19 Jun 2003
AB Background: LIM mineralization protein-1 (***LMP*** - ***1***), an intracellular protein, is thought to induce secretion of soluble factors that convey its osteoinductive activity. Although evidence suggests that ***LMP*** - ***1*** may be a critical regulator of ***osteoblast*** ***differentiation*** in vitro and in vivo, little is known about its mechanism of action. The purpose of the present study was to identify candidates for the induced secreted factors and to describe the time sequence of histological changes during bone formation induced by ***LMP*** - ***1*** . Methods: Human lung carcinoma (A549) cells were used to determine if ***LMP*** - ***1*** overexpression would induce expression of bone morphogenetic proteins (BMPs) in vitro. Cultured A549 cells were infected with recombinant replication-deficient human type-5 adenovirus containing the ***LMP*** - ***1*** or LacZ cDNA. Cells were subjected to immunohistochemical analysis after forty-eight hours. Finally, sixteen athymic rats received subcutaneous implants consisting of collagen disks loaded with human buffy-coat cells that were infected with one of the above two viruses. Rats were killed at intervals, and explants were studied with histological and immunohistochemical analyses. Results: In vitro experiments with A549 cells showed that AdLMP-1-infected cells express elevated levels of BMP-2, BMP-4, BMP-6, BMP-7, and TGF-.beta.1 (transforming growth factor-beta 1) protein. Human buffy-coat cells infected with AdLMP-1 also demonstrated increased levels of BMP-4 and BMP-7 protein seventy-two hours after ectopic implantation in athymic rats, confirming the in vitro hypothesis. Conclusions: The osteoinductive properties of ***LMP*** - ***1*** involve synthesis of several BMPs and the recruitment of host cells that differentiate and participate in direct membranous bone formation. Clinical Relevance: Ex vivo gene therapy with the ***LMP*** - ***1*** cDNA-induced secretion of multiple BMPs may provide an alternative to implantation of large doses of a single BMP to induce new bone formation.

L27 ANSWER 12 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2003:432263 BIOSIS <<LOGINID::20071018>>
DN PREV200300432263
TI The involvement of ***LMP*** - ***1*** in prostate cancer metastasis to bone.
AU Hair, G. A. [Reprint Author]; Titus, L.; Boden, S. D. [Reprint Author]
CS Orthopaedics, Emory University, Atlanta, GA, USA
SO Journal of Bone and Mineral Research, (September 2002) Vol. 17, No. Suppl 1, pp. S411. print.
Meeting Info.: Twenty-Fourth Annual Meeting of the American Society for Bone and Mineral Research. San Antonio, Texas, USA. September 20-24, 2002.
American Society for Bone and Mineral Research.
ISSN: 0884-0431 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003

L27 ANSWER 13 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 3

AN 2002:314563 BIOSIS <<LOGINID::20071018>>
DN PREV200200314563
TI Dexamethasone inhibits osteoblastic differentiation by down-regulation of LIM mineralization protein 1.
AU Liu Su-Cai [Reprint author]; Zhang Zhi-Yong; Li En
CS Department of Biochemistry, Hebei Medical University, Shijiazhuang, 050017, China
liusucai@163.net
SO Shengli Xuebao, (February 25, 2002) Vol. 54, No. 1, pp. 33-37. print.
CODEN: SLHPAH. ISSN: 0371-0874.
DT Article
LA Chinese
ED Entered STN: 29 May 2002
Last Updated on STN: 29 May 2002
AB To investigate the mechanisms of the inhibition of osteoblastic differentiation by dexamethasone (DEX), the effects of different doses of DEX on the activity of alkaline phosphatase (ALP), the synthesis of osteocalcin (OC) and the expression of colaggen type I were observed in the cultured rat osteoblasts. The LIM mineralization protein-1 (***LMP*** - ***1***) mRNA, a positive regulator of osteoblasts, was semi-quantified by RT-PCR. The results showed that a lower dose (10-9 mol/L) of DEX could enhance the activity of ALP, the synthesis of OC and the expression of collagen type I. However, a higher dose (10-7 mol/L) of DEX inhibited them and down-regulated the expression of ***LMP*** - ***1*** mRNA in osteoblasts. It is suggested that DEX stimulates ***osteoblast*** ***differentiation*** at lower dose, while at higher dose it inhibits ***osteoblast*** ***differentiation*** . The inhibitory action of DEX on ***osteoblast*** ***differentiation*** might be mediated by the down-regulation of ***LMP*** - ***1*** mRNA.

L27 ANSWER 14 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 4
AN 2000:509866 BIOSIS <<LOGINID::20071018>>
DN PREV200000509866
TI Inhibition of ***osteoblast*** ***differentiation*** by tumor necrosis factor-alpha.
AU Gilbert, Linda; He, Xiaofei; Farmer, Paul; Boden, Scott; Kozlowski, Mirek; Rubin, Janet; Nanes, Mark S. [Reprint author]
CS VA Medical Center, 1670 Clairmont Road, Decatur, GA, 30033, USA
SO Endocrinology, (November, 2000) Vol. 141, No. 11, pp. 3956-3964. print.
CODEN: ENDOAO. ISSN: 0013-7227.
DT Article
LA English
ED Entered STN: 22 Nov 2000
Last Updated on STN: 11 Jan 2002
AB Tumor necrosis factor-alpha (TNF-alpha) has a key role in skeletal disease in which it promotes reduced bone formation by mature osteoblasts and increased osteoclastic resorption. Here we show that TNF inhibits differentiation of osteoblasts from precursor cells. TNF-alpha treatment of fetal calvaria precursor cells, which spontaneously ***differentiate*** to the ***osteoblast*** phenotype over 21 days, inhibited differentiation as shown by reduced formation of multilayered, mineralizing nodules and decreased secretion of the skeletal-specific matrix protein osteocalcin. The effect of TNF was dose dependent with an IC50 of 0.6 ng/ml, indicating a high sensitivity of these precursor cells. Addition of TNF-alpha from days 2-21, 2-14, 7-14, and 7-10 inhibited nodule formation but addition of TNF after day 14 had no effect. Partial inhibition of differentiation was observed with addition of TNF on only days 7-8, suggesting that TNF could act during a critical period of phenotype selection. Growth of cells on collagen-coated plates did not prevent TNF inhibition of differentiation, suggesting that inhibition of collagen deposition into matrix by proliferating cells could not, alone, explain the effect of TNF. Northern analysis revealed that TNF inhibited the expression of insulin-like growth factor I (IGF-I). TNF had no effect on expression of the osteogenic bone morphogenic proteins (BMPs-2, -4, and -6), or skeletal LIM protein (***LMP*** - ***1***), as determined by semiquantitative RT-PCR. Addition of IGF-I or BMP-6 to fetal calvaria precursor cell cultures enhanced differentiation but could not overcome TNF inhibition, suggesting that TNF acted downstream of these proteins in the differentiation pathway. The clonal osteoblastic cell line, MC3T3-E1-14, which acquires the osteoblast phenotype spontaneously in postconfluent culture, was also studied. TNF inhibited differentiation of MC3T3-E1-14 cells as shown by failure of mineralized matrix formation in the presence of calcium and phosphate. TNF was not cytotoxic to either cell type as shown by continued attachment and metabolism in culture, trypan blue exclusion, and Alamar Blue cytotoxicity assay. These results demonstrate that TNF-alpha is a potent inhibitor of ***osteoblast*** ***differentiation*** and suggest that TNF acts distal to IGF-I, BMPs, and ***LMP*** - ***1*** in the progression toward the osteoblast phenotype.

L27 ANSWER 15 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 5
AN 2000:445619 BIOSIS <<LOGINID::20071018>>
DN PREV200000445619
TI Biology of lumbar spine fusion and use of bone graft substitutes: Present, future, and next generation.
AU Boden, Scott D. [Reprint author]
CS Department of Orthopaedic Surgery, Emory Spine Center, Emory University School of Medicine, 2165 N. Decatur Rd., Decatur, GA, 30033, USA
SO Tissue Engineering, (August, 2000) Vol. 6, No. 4, pp. 383-399. print.
ISSN: 1076-3279.
DT Article
LA English
ED Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002
AB Posterolateral lumbar spine arthrodesis is a commonly performed procedure, yet the biology of healing is poorly understood. Nonunion, or failure to achieve a solid bony fusion, occurs in up to 40% of patients. We first developed and validated a rabbit model to characterize the healing process by measuring macroscopic parameters, microscopic parameters, and gene expression. We found that presently available osteoconductive and weakly osteoinductive materials were insufficient to replace autografts, but could in some cases serve as bone graft extenders. In contrast, two osteoinductive growth factors currently in development could replace autograft in non-human primates and in humans, but may be limited by the high dose required, carrier variability, and high cost. We identified, cloned, and sequenced a novel complementary DNA (cDNA) encoding for an intracellular protein ***LMP*** - ***1*** , which is expressed during the first few hours of ***osteoblast*** ***differentiation*** . ***LMP*** - ***1*** expression is able to induce many BMPs, their receptors, and other bone growth factors. Local implantation of bone marrow cells transfected with ***LMP*** - ***1*** cDNA induced spine fusion in 100% of sites tested; no bone formed at the control sites without ***LMP*** - ***1*** . This strategy of local gene therapy may provide a basis for the next generation of bone graft substitutes.

L27 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 6
AN 1999:36298 BIOSIS <<LOGINID::20071018>>
DN PREV199900036298
TI ***LMP*** - ***1*** : A LIM-domain protein, mediates BMP-6 effects on bone formation.
AU Boden, Scott D. [Reprint author]; Liu, Yunshan; Hair, Gregory A.; Helms, Jill A.; Hu, Diane; Racine, Michele; Nanes, Mark S.; Titus, Louisa
CS Emory Spine Cent., 2165 North Decatur Rd., Decatur, CA 30033, USA
SO Endocrinology, (Dec., 1998) Vol. 139, No. 12, pp. 5125-5134. print.
CODEN: ENDOAO. ISSN: 0013-7227.
DT Article
LA English
ED Entered STN: 3 Feb 1999
Last Updated on STN: 3 Feb 1999
AB Glucocorticoids can promote ***osteoblast*** ***differentiation*** from fetal calvarial cells and bone marrow stromal cells. We recently reported that glucocorticoid specifically induced bone morphogenetic protein-6 (BMP-6), a glycoprotein signaling molecule that is a multifunctional regulator of vertebrate development. In the present study, we used fetal rat secondary calvarial cultures to determine genes induced during early ***osteoblast*** ***differentiation*** as initiated by glucocorticoid treatment. Glucocorticoid, and subsequently BMP-6, was found to induce a novel rat intracellular protein, LIM mineralization protein-1 (***LMP*** - ***1***), that in turn resulted in synthesis of one or more soluble factors that could induce de novo bone formation. Blocking expression of ***LMP*** - ***1*** using antisense oligonucleotide prevented ***osteoblast*** ***differentiation*** in vitro. Overexpression of ***LMP*** - ***1*** using a mammalian expression vector was sufficient to initiate de novo bone nodule formation in vitro and in sc implants in vivo. These data demonstrate that ***LMP*** - ***1*** is an essential positive regulator of the ***osteoblast*** ***differentiation*** program as well as an important intermediate step in the BMP-6 signaling pathway.

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